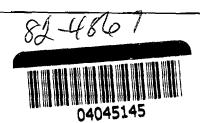


amrad corporation limited abn 37 006 614 375 576 swan street richmond victoria australia 3121 telephone (61 3) 9208 4000 facsimile (61 3) 9208 4356 http://www.amrad.com.au



To:

The Securities and Exchange Commission

Company:

Fax:

0011 1 202 942 9624

From:

Robyn Fry - Company Secretary

Fax:

(+61 3) 9208 4356

Date:

27 September 2004

Pages:

Including cover page

5

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MINISTER 28 P 1: U

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# **FACSIMILE COVER SHEET**

# Amrad Corporation Limited

Please find attached information being furnished by Amrad Corporation Limited to the Securities and Exchange Commission.

P.P. 12ther

Robyn Fry

General Counsel & Company Secretary

**PROCESSED** 

SEP 2 9 2004

> THOMSON FINANCIAL

Doc# 105059 v1

amrad-#105059-v1-securities\_exchange\_commission\_(sec)\_fax.doc
A biotechnology research & development company Page I of I



amrad corporation limited abn 37 006 614 375 576 swan street richmond victoria australia 3121

telephone (61 3) 9208 4000 facsimile (61 3) 9208 4356 http://www.amrad.com.au

27 September 2004

Securities and Exchange Commission Division of Corporate Finance 450 Fifth Street NW WASHINGTON DC 20549 USA

Dear Sirs

AMRAD Corporation Limited Rule 12g3-2(b) Exemption (File No. 82-4867)

The enclosed information is being furnished by AMRAD Corporation Limited ("AMRAD") under paragraph (b)(1)(i) of Rule 12g3-2 under the Securities Exchange Act of 1934 ("the Exchange Act"). AMRAD's file number is indicated in the upper right hand corner of each unbound page and the first page of each bound document furnished herewith.

In accordance with paragraphs (b)(4) and (b)(5) of the Rule, the documents furnished herewith are being furnished with the understanding that such documents will not be deemed "filed" with the Securities and Exchange Commission or otherwise subject to the liabilities of Section 18 of the Exchange Act, and that neither this letter nor the furnishings of such documents shall constitute an admission for any purpose that AMRAD is subject to the Exchange Act.

Yours sincerely

Robyn Fry

General Counsel & Company Secretary

Doc# 106999 v1

# Rule 12g3-2(b) Card Received from the SEC

ISSUER AMRAO	Corporation Limited	EILE NO. 82- 4867
9/4/98		

This will advise that the issuer has been added to the list of those foreign private issuers that claim exemption pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Please be further advised that in order to continue to daim this exemption, the issuer must furnish to the Commission, on a timely basis, all information required by Rule 12g3-2(b). This includes all relevant documents since the date of your initial submission. The burden of furnishing such information rests with the issuer, even if it delegates that responsibility to another, and the staff will look to the issuer for compliance. If the issuer is a member of an affiliated or control group which normally prepares reports, press releases, etc., in a single document, a separate report must be submitted for each issuer that claims an exemption under the rule because separate files are maintained for each issuer.

ALL FUTURE SUBMISSIONS MUST PROMINENTLY INDICATE THE EXEMPTION NUMBER IN THE UPPER RIGHT HAND CORNER OF EACH UNBOUND PAGE AND THE FIRST PAGE OF EACH BOUND DOCUMENT PURSUANT TO THE IDENTIFICATION PROVISIONS OF THE RULE. FAILURE TO SO INDICATE WILL RESULT IN THE SUBMISSION BEING RETURNED TO THE SENDER AND THE SUBMISSION NOT BEING RECORDED, RESULTING IN POSSIBLE LOSS OF THE EXEMPTION.

# **Nicky Haw**

From:

Sent:

To:

ASX.Online@asx.com.au Monday, 27 September 2004 9:53 rfry@amrad.com.au; nhaw@amrad.com.au

Subject:

AML - ASX Online e-Lodgement - Confirmation of Release



ASX confirms the release to the market of Doc ID: 166809 as follows; Release Time: 27-Sep-2004 09:52:34 ASX Code: AML File Name: 166809.pdf Your Announcement Title: AMRAD SHARE BUY-BACK PROGRAM TO RESUME



amrad corporation limited abn 37 006 614 375 576 swan street richmond victoria australia 3121 telephone (61 3) 9208 4320 facsimile (61 3) 9208 4352 http://www.amrad.com.au

27 September 2004

#### AMRAD SHARE BUY-BACK PROGRAM TO RESUME

Amrad Corporation Limited (ASX:AML) announced today the decision to resume the share buy-back that was initiated by the Company in April 2004.

The buy-back program in respect of up to 10% of Amrad's fully paid ordinary shares was suspended by the Amrad Board in July 2004 to enable the calculation of entitlements of Amrad shareholders for the purposes of the demerger of the Company's anti-infectives business, Avexa Limited.

Commenting on the resumption of the buy-back program Amrad Chairman, Mr Bob Moses, explained "Following the successful completion of the Avexa demerger and spin-out and the subsequent ASX listing of Avexa on 23 September the Board has determined it is now appropriate to recommence the buy-back program."

For further information contact:

Or Pete Smith Chief Executive Officer Telephone: 61 3 9208 4108

For additional company information refer to Amrad's website:

www.amrad.com.au

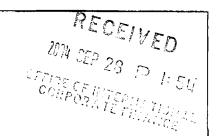
Doc# 122689 v3

A blotechnology research & development company

Page 1 of 1



amrad corporation limited abn 37 006 614 375 576 swan street richmond victoria australia 3121 telephone (61 3) 9208 4000 facsimile (61 3) 9208 4356 http://www.amrad.com.au



To:

The Securities and Exchange Commission

Company:

Fax:

0011 1 202 942 9624

From:

Robyn Fry - Company Secretary

Fax:

(+61 3) 9208 4356

Date:

22 September 2004

Pages:

13

Including cover page

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# FACSIMILE COVER SHEET

# **Amrad Corporation Limited**

Please find attached information being furnished by Amrad Corporation Limited to the Securities and Exchange Commission.

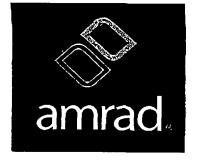
Robyn Fry

General Counsel & Company Secretary

Doc# 105059 v1

amrad-#105059-v1-securities\_exchange\_commission\_(sec)\_fax.doc A biotechnology research & development company

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amrad corporation limited abn 37 006 614 375 576 swan street richmond victoria australia 3121

telephone (61 3) 9208 4000 facsimile (61 3) 9208 4089 http://www.amrad.com.au

22 September 2004

Securities and Exchange Commission Division of Corporate Finance 450 Fifth Street NW WASHINGTON DC 20549 USA

Dear Sirs

AMRAD Corporation Limited Rule 12g3-2(b) Exemption (File No. 82-4867)

The enclosed information is being furnished by AMRAD Corporation Limited ("AMRAD") under paragraph (b)(1)(i) of Rule 12g3-2 under the Securities Exchange Act of 1934 ("the Exchange Act"). AMRAD's file number is indicated in the upper right hand corner of each unbound page and the first page of each bound document furnished herewith.

In accordance with paragraphs (b)(4) and (b)(5) of the Rule, the documents furnished herewith are being furnished with the understanding that such documents will not be deemed "filed" with the Securities and Exchange Commission or otherwise subject to the liabilities of Section 18 of the Exchange Act, and that neither this letter nor the furnishings of such documents shall constitute an admission for any purpose that AMRAD is subject to the Exchange Act.

Yours sincerely

Robyn Fry

General Counsel & Company Secretary

Doc# 106999 v1

# Rule 12g3-2(b) Card Received from the SEC

AMRAO Corporation Limited	FILE NO. 82- 4867
9 4 98	

This will advise that the issuer has been added to the list of those foreign private issuers that claim exemption pursuant to Rule 12g3-Z(b) under the Securities Exchange Act of 1934.

Please be further advised that in order to continue to claim this exemption, the issuer must furnish to the Commission, on a timely basis, all information required by Rule 12g3-2(b). This includes all relevant documents since the date of your initial submission. The burden of furnishing such information rests with the issuer, even if it delegates that responsibility to another, and the staff will look to the issuer for compliance. If the issuer is a member of an affiliated or control group which normally prepares reports, press releases, etc., in a single document, a separate report must be submitted for each issuer that claims an exemption under the rule because separate files are maintained for each issuer.

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AUSTRALIAN STOCK EXCHANGE



Australian Stock Exchange Limited ABN 98 008 624 691 Exchange Centre Level 4, 20 Bridge Street Sydney NSW 2000

PO Box H224 Australia Square NSW 1215

Telephone 61 2 9227 0334

Internet http://www.asx.com.au DX 10427 Stock Exchange Sydney

**FACSIMILE** 

Department: COMPANY ANNOUNCEMENTS OFFICE

DATE:

20/09/2004

TIME:

18:04:19

TO:

AMRAD CORPORATION LIMITED

FAX NO:

03-9208-4356

FROM:

AUSTRALIAN STOCK EXCHANGE LIMITED - Company Announcements Office

SUBJECT:

CONFIRMATION OF RECEIPT AND RELEASE OF ANNOUNCEMENT

### MESSAGE:

We confirm the receipt and release to the market of an announcement regarding:

Notice of Annual General Meeting

# PLEASE NOTE:

In accordance with Guidance Note 14 of ASX Listing Rules -

OΤ

- Use of ASX Online for lodgement of company announcements becomes mandatory from <u>1 July 2003</u>
- Handwritten and hand-delivered company announcements are no longer accepted
- Fee of A\$38.50 (including GST) applies from <u>1 March 2003</u> for announcements <u>faxed</u> to CAP
- New CAP fax number from 1 March 2003 for announcements sent within Australia is 1900 999 279



# Robyn Fry

From:

ASX.Online@asx.com.au

Sent:

Monday, 20 September 2004 18:04

To:

Subject:

rfry@amrad.com.au; nhaw@amrad.com.au AML - ASX Online e-Lodgement - Confirmation of Release



165221.pdf (99 KB)

ASX confirms the release to the market of Doc ID: 165221 as follows: Release Time: 20-Sep-2004 18:04:17 ASX Code: AML File Name: 165221.pdf Your Announcement Title: Amrad 2004 Notice of Annual General Meeting





# Amrad Corporation Limited - Notice of Annual General Meeting - Thursday, 21 October 2004

Notice is given that the 18th Annual General Meeting of the Company will be held at Computershare Conference Centre, Yarra Falls, 452 Johnston Street, Abbotsford, Victoria, Australia on Thursday, 21 October 2004 at 11,00am.

### Ordinary Business

#### Consideration of Reports

To receive and consider the Financial Report of the Company, the Directors' Report and the Auditor's Report, for the year ended 30 June 2004.

#### 2. Re-election of Director

To re-elect a Director:

Mr Robert William Moses retires in accordance with Rule 58 of the Constitution and, being eligible, offers himself for re-election.

#### Election of Director

To elect a Director:

Dr Peter Smith retires in accordance with Rule 47 of the Constitution and, being eligible, affers himself for election.

#### Special Business

### 4. Approval of Issue of Options to Chief Executive Officer

To consider and, if thought fit, pass the following resolution as an ordinary resolution:

"That approval be given to the issue to Dr Peter Smith, the Chief Executive Officer and Executive Director of the Company. of 600,000 options (each option conferring a right to subscribe for one fully paid ordinary share in the capital of the Company) on the terms set out in the Explanatory Notes to this Notice of Meeting."

#### 5. Approval of Further Issue of Options to Chief Executive Officer

To consider and, if thought fit, pass the following resolution as an ordinary resolution:

"That approval be given to the issue to Dr Peter Smith, the Chief Executive Officer and Executive Director of the Company, of 400,000 options (each option conferring a right to subscribe for one fully paid ordinary share in the capital of the Company) on the terms set out in the Explanatory Notes to this Notice of Meeting."

# 6. Approval of Issue of Options under ASX Listing Rule 7.2 Exception 9

To consider and, if thought fit, pass the following resolution as an ordinary resolution:

"That for the purpose of ASX Listing Rule 7.2 Exception 9, approval be given to the issue of options referred to in Resolutions 4 and 5 to the Chief Executive Officer and Executive Director under the Option Incentive Plan and Key Employee Share Option Plan described in the Explanatory Notes to this Notice of Meeting as an exception to Listing Rule 7.1.

#### **Proxies**

Please note that:

- (a) a member of the Company entitled to attend and vote at the Annual General Meeting has the right to appoint a proxy;
- (b) a proxy need not be a member of the Company; and
- (c) a member who is entitled to cast two or more votes may appoint two proxies and may specify the proportion or number of votes each proxy is appointed to exercise.

<sup>2</sup> Amrad Corporation - Notice of Annual General Meeting

Tile No.,

A form of proxy accompanies this Notice of Armual General Meeting. For the appointment of a proxy to be effective for a meeting. the following documents must be received by the Company or Computershare Investor Services Pty Limited at least 48 hours before the meeting:

- (a) the proxy's appointment; and
- (b) if the appointment is signed by the appointor's attorney the authority under which the appointment was signed or a certified copy of the authority.

Documents may be lodged using the reply paid envelope provided or:

- by posting, delivery or facsimile to the Company's share registry at:
  - Amrad Corporation Limited share registry Computershare Investor Services Pty Limited GPO Box 242

Melbourne Victoria 3001 Australia

Facsimile: 61 3 9473 2555 or,

· by posting, delivery or facsimile to the Registered Office of the Company at:

Amrad Corporation Limited 576 Swan Street Richmond Victoria 3121 Australia

Facsimile: 61 3 9208 4356

### Voting Entitlement

Pursuant to Reg 7.11.37 of the Corporations Regulations 2001 (Cth) for the purposes of the meeting, persons holding shares at 11.00am on 18 October 2004 will be treated as shareholders. This means that if you are not the registered holder of a relevant share at that time you will not be entitled to vote in respect of that share.

By order of the Board

Company Secretary Amrad Corporation Limited

Dated 17 September 2004

# **EXPLANATORY NOTES**



#### Resolution 2 - Re-election of Director

Candidate for re-election to the office of Director:

## Mr Bob Moses (Chairman) MBA (University of Chicago), Age 65

Bob Moses joined the Amrad Board in May 2002 and was appointed Chairman in October 2003. Retired Vice President of CSI, Limited, Mr Moses draws on more than 35 years in the global pharmaceutical industry. For the eight years preceding retirement, his specific responsibilities were focussed on growth and development of CSL's international businesses and global commercial relationships. His accomplishments include negotiating commercial agreements and alliances with major multinational pharmaceutical. votorinary companies, biotechnology companies and research institutions as well as key roles in acquisition and development of certain of the Company's international businesses. Prior to joining CSL. Mr Mosos was Managing Director of commercial law firm Freehills, Chairman and CEO of a NASDAQ listed medical service company and Corporate Manager of new Business Development at ICI (now Orica). He also spent 17 years in various management roles at the multinational pharmaceutical company. Eli Lilly. Mr Moses is Chairman of the Biotechnology Centre of Excellence for Stem Cell and Tissue Repair, Chairman of Meditech Research Limited, Chairman of the CRC for Inflammatory Diseases and Chairman of Antisense Therapeutics Limited. Mr Moses is Senior Consultant to The Murdoch Children's Research Institute and a Follow of the Australian Institute of Company Directors and the Australian Institute of Management.

#### Resolution 3 - Election of Director

Candidate for election to the office of Director:

### Dr Peter Smith (CEO and Executive Director) MA (Cambridge) PhD, Age 41

Dr Smith was appointed to the chief executive role at Amrad in October 2003. He is a former international investment bank analyst and co-founder and director of London based Onyvax, a private UK biotechnology company specialising in cancer immunotherapy R&D.

Dr Smith spent nine years as a top rated analyst for investment banks UBS and HSBC covering the European pharmaceutical/ biotech industry. His PhD is in the area of cell signalling. Dr Smith combines a detailed knowledge of laboratory and clinical environments, with the strong corporate and financial management experience required for success in today's biotech company.

### Resolution 4 - Approval of Issue of Options to Chief Executive Officer

The appointment of Dr Smith as the Company's new Chief Executive Officer is described in the Explanatory Notes to Resolution 3.

Attracting an executive of Dr Smith's calibre involved careful consideration of an appropriate remuneration package. The Executive Service Agreement that has been entered into by the Company and Dr Smith includes short and long term incentive components designed to align the Chief Executive Officer's interests with those of the Company. The Company sought and followed external professional advice on these matters. The long term incentives proposed by the Board involve the issue of options over ordinary shares in Amrad on certain terms and conditions (such terms and conditions are referred to in these Explanatory Notes as the "Option Incentive Plan"). Specifically, the exercise price of the options as set out below has been determined with a view to reflecting substantial benefits to shareholders.

Pursuant to the ASX Listing Rules, shareholders are required to approve the issue of options to a Director under an employee incentive scheme. Accordingly, Resolution 4 is to approve the issue to Dr Smith of 600,000 options to subscribe for ordinary shares in the capital of the Company through the Option Incentive Plan. If shareholders do not approve the issue of these options, the Company is required to ensure that Dr Smith is provided with alternative benefits of an equivalent after tax value to him.

In respect of the proposed issue of options under the Option Incentive Plan, the following information is provided in accordance with the ASX Listing Rules.

A summary of the key terms of the options that are proposed to be issued to Dr Smith is set out below. The Option incentive Plan that has been developed for Dr Smith replicates the Amrad Key Employee Share Option Plan (the "KESOP") except as provided in paragraph (b) below. Dr Smith is the only person who is entitled to participate in the Option Incentive Plan.

4 Amrad Corporation - Notice of Annual General Meeting

#### (a) Number and Exercise Price of Options

Under the Option Incentive Plan, Dr Smith will be offered 600,000 options. Dr Smith will not be required to pay any consideration to Amrad for the options. Each option will confer a right to subscribe for one fully paid ordinary share in Amrad at the exercise price of \$1,15.

#### (b) Exercise of Options

- (i) The options to be offered to Dr Smith will be divided into three tranches of 200,000 options. Except as provided in paragraph (ii) below, none of the options will be capable of exercise unless Dr Smith is the Chief Executive Officer of the Company at all times up to and including 16 October 2004 (which is the first anniversary of the commencement of his employment with Amrad). The tranches of options will be exercisable (subject to paragraph (ii) below) as follows:
  - (a) 200,000 options exercisable within three years after 16 October 2004;
  - (b) 200,000 options exercisable within three years after 16 October 2005; and
  - (c) 200,000 options exercisable within three years after 16 October 2006.

Subject to paragraph (ii) below, options that are not exercised prior to the end of the relevant three year period referred to above will lapse at the end of that period.

(ii) If Dr Smith's employment is terminated by Amrad otherwise than for misconduct, bankruptcy or becoming disqualified from holding the office of director under the Corporations Act, Dr Smith or his estate will be entitled to exercise any options that are then exercisable and a proportional amount (determined by the Amrad Board) of any other options based on the length of time that he had served as Chief Executive Officer of Amrad.

If his employment terminates due to misconduct, bankruptcy or becoming disqualified from holding the office of Director under the Corporations Act, Dr Smith will not be entitled to exercise any of the options and they will lapse immediately. If Dr Smith resigns, any options that are then exercisable will continue to be exercisable and any other options will lapse immediately.

In addition, if all or substantially all of the undertaking and assets of the Company are sold or the Company becomes a subsidiary of another entity, Dr Smith will be entitled to exercise all of the options (whether or not they otherwise would then be exercisable).

# (c) Summary of the Terms of the KESOP That Apply to the Option Incentive Plan

#### (i) Lapse of Options:

The options will lapse if not exercised on or before the first to occur of any default by Dr Smith under the Rules of the KESOP that are applicable to the Option Incentive Plan, insolvency of Amrad, and other defined events associated with an insolvency of Amrad.

#### (ii) Restrictions on Transfers:

The options may be transferred or assigned to an associated trust or to a spouse of Dr Smith if the Amrad Board, in its absolute discretion, approves the transfer and the transferree has agreed to be bound by the terms on which the options were issued and the Option Incentive Plan (including the applicable Rules of the KESOP).

#### (iii) Bonus Issues:

On any bonus issue, there will be a corresponding increase in the number of underlying shares to which Dr Smith's options relate. This will not affect the total amount payable upon the exercise of Dr Smith's options.

### (iv) Rights Issues:

Dr Smith cannot participate in a rights issue in respect of any unexercised options. However, the exercise price will be reduced by an amount equal to the theoretical value of the rights entitlement determined in accordance with the ASX Listing Rules.

### (v) Reconstructions:

Any reconstruction of capital (such as consolidation, subdivision, reduction or return of capital) will result in a corresponding adjustment to the number of options or to the exercise price or both so as to preserve Dr Smith's proportionate entitlement. The options are also to be reconstructed in accordance with the ASX Listing Rules, as amended from time to time over the course of the Option Incentive Plan.

Amrad Corporation - Notice of Annual General Meeting 5

# **EXPLANATORY NOTES**

CONTINUED



### (vi) Issue of Shares Upon Exercise of Options:

On the exercise of the options, Amrad will issue the applicable number of ordinary shares, and will apply for quotation of those shares on the ASX. The shares issued will rank equally with other fully-paid ordinary shares in Amrad.

Shareholders may inspect a copy of the full terms of the KESOP at Computershare Investor Services Pty Ltd during normal business hours or on the Company's website (http://www.amrad.com.au).

Details of the options issued under the Option Incentive Plan will be published in each Annual Report of Amrad relating to the period in which the options were issued. Approval for the issue of those options will have been obtained under ASX Listing Rule 10.14. If Amrad's shareholders approve Resolution 4, Amrad will offer the options to Dr Smith (and, if the offer is accepted, issue them to him) as soon as practicable after the Annual General Meeting, but in any event no later than three years after the Annual General Meeting.

The ASX Listing Rules require the Company to disregard votes cast on this resolution by any Director of the Company eligible to participate in any employee incentive scheme. Accordingly, the Company will disregard any votes cast on this resolution by any Director of the Company, or any associates of those persons, other than a vote cast by:

- (f) such a person as proxy for a person who is entitled to vote, in accordance with the directions on the proxy form; or
- (ii) such a person as chairman of the meeting as proxy for a person who is entitled to vote, in accordance with a direction on the proxy form to vote as the proxy decides.

# Resolution 5 - Approval of Further Issue of Options to Chief Executive Officer

As outlined above in the Explanatory Notes to Resolution 4, the ASX Listing Rules require shareholders to approve the issue of options to a Director under an employee incentive scheme. Accordingly, Resolution 5 is to approve the issue to the Chief Executive Officer Dr Smith of a further 400,000 options to subscribe for ordinary shares in the capital of the Company.

Corporate performance targets were established for Dr Smith as part of his remuneration arrangements. If satisfied, Dr Smith will become crititled to specified remuneration increases and options to acquire ordinary shares in the capital of the Company exercisable within five years of the date on which the options are granted. As part of these remuneration arrangements, the Amrad Board has proposed that, in respect of the financial year ended 30 June 2004, Dr Smith be issued up to a maximum of 400,000 options pursuant to the terms of the Amrad Key Employee Share Option Plan (the "KESOP"), except as described in paragraph (b) below. to acquire fully paid ordinary shares in the capital of the Company.

A summary of the key terms of the options that are proposed to be issued to Dr Smith is set out below accordance with the ASX Listing Rules.

### (a) Number of Options

Or Smith will be offered 400,000 options and will not be required to pay any consideration to Amrad for the options. Each option will confer a right to subscribe for one fully paid share in Amrad.

## (b) Exercise Price of Options

The price payable on exercise of the options to acquire Amrad shares is to be an amount equal to 110 per cent of the market value of an Amrad share on the issue date. Market value will be calculated in accordance with the income Tax Assessment Act formula, by reference to the weighted average price of sales of Amrad shares on the stock market of the Australian Stock Exchange Limited during the one week period up to and including the issue date.

### (c) Exercise and Lapse of Options

The options to be offered to Dr Smith will be exercisable within five years of the date of issue and will lapse if not exercised on or before the first to occur of the following:

- (i) the expiration of five years after the date the options were granted:
- (ii) the expiration of 12 months after the death or permanent disablement of the participant;
- (iii) immediately on termination of employment involving misconduct;
- (iv) default by the participant under the Rules of the KESOP;
- (v) the expiration of 60 days after the option is transferred; and
- (vi) other defined events associated with insolvency of Amrad.

6 Arnrad Corporation - Notice of Annual General Meeting



As an Executive Director, under the KESOP Dr Smith would be entitled to retain any options issued which have not been exercised at the time of cossation of his employment unless such cossation of employment occurs as a result of fraud, dishonesty or misconduct.

A summary of the terms of the KESOP that apply to the proposed issue of options to Dr Smith pursuant to both Resolutions 4 and 5 is set out in paragraph (c) of the Explanatory Notes to Resolution 4.

Shareholders may inspect a copy of the full terms of the KESOP at Computershare Investor Services Pty Ltd during normal business hours or on the Company's website (http://www.amrad.com.au).

Details of the options issued under the Amrad KESOP to Dr Smith will be published in each Annual Report of Amrad relating to the period in which the options were issued. Approval for the issue of those options will have been obtained under ASX Listing Rule 10.14.

If Amrad's shareholders approve Resolution 5, Amrad will offer the options to Dr Smith (and, if the offer is accepted, issue them to him) as soon as practicable after the Annual General Meeting, but in any event no later than three years after the Annual General

Other than Dr Smith, no Director, or associate of a Director, of Amrad has been issued options under the KESOP since the 2002 Annual General Meeting of the Company.

The ASX Listing Rules require the Company to disregard votes cast on this resolution by any Director of the Company eligible to participate in any employed incentive scheme. Accordingly, the Company will disregard any votes cast on this resolution by any Director of the Company, or any associates of those persons, other than a vote cast by:

- (i) such a person as proxy for a person who is ontitled to vote, in accordance with the directions on the proxy form; or
- (ii) such a person as chairman of the meeting as proxy for a person who is entitled to vote, in accordance with a direction on the proxy form to vote as the proxy decides.

## Resolution 6 - Approval of Issue of Options under ASX Listing Rule 7.2 Exception 9

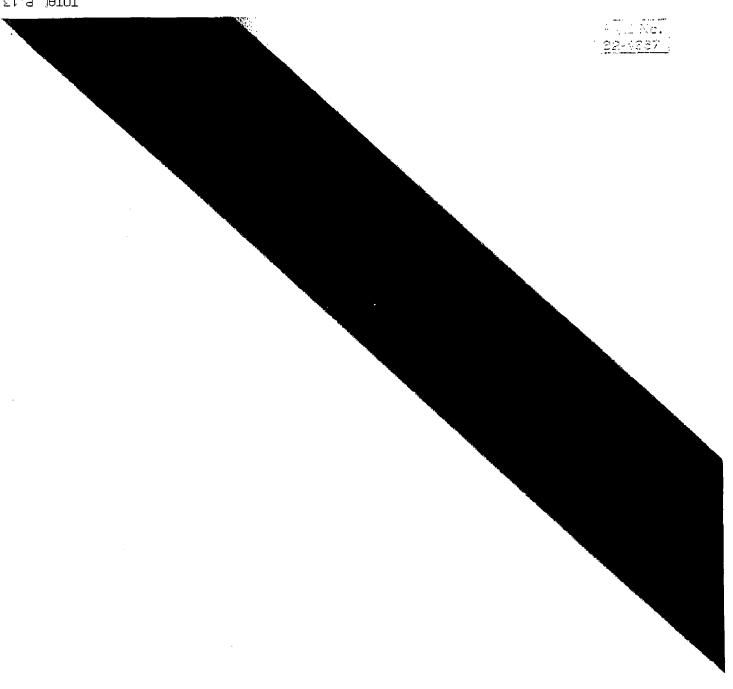
Listing Rule 7.1 requires a company to obtain the approval of shareholders if it wishes to be free to issue more than 15 per cent of its capital within a 12 month period. Listing Rule 7.2 contains a number of exceptions to Listing Rule 7.1, allowing certain issues of securities to be excluded from calculations of the number of equity securities issued in the preceding 12 months. Shareholder approval under Listing Rule 7.2 (Exception 9) of the options to be issued to Dr Smith under the Option Incentive Plan and the Key Employee Share Option Plan (the "KESOP") pursuant to Resolutions 4 and 5 respectively would enable the issue of those options in the next three years, and any shares issued upon the exercise of those options, to be excluded from such calculations.

Summaries of the terms of the Option Incentive Plan and the KESOP are contained in the Explanatory Notes to Resolution 4. No options have yet been issued to Dr Smith under either the Option Incentive Plan or the KESOP.

The ASX Listing Rules require the Company to disregard votes on this resolution by any Director of the Company eligible to participate in any employee incentive scheme. Accordingly, the Company will disregard any votes cast on this resolution by any Director of the Company, or any associates of those persons, other than a vote cast by:

- (i) such a person as proxy for a person who is entitled to vote, in accordance with the directions on the proxy form; or
- (ii) such a person as chairman of the meeting as proxy for a person who is entitled to vote, in accordance with a direction on the proxy form to vote as the proxy decides.

Anirad Corporation - Notice of Annual General Meeting 7





Amrad Corporation Limited ABN 37 006 614 375 576 Swan Street Richmond Victoria Australia 3121 Telephone (61-3) 9208 4000 Facsimile (61-3) 9208 4356 www.amrad.com.au

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OT



amrad corporation limited abn 37 006 614 375 576 swan street richmond victoria australia 3121 telephone (61 3) 9208 4000 facsimile (61 3) 9208 4356 http://www.amrad.com.au

To:

The Securities and Exchange Commission

Company:

Fax:

0011 1 202 942 9624

From:

Robyn Fry - Company Secretary

Fax:

(+61 3) 9208 4356

Date:

22 September 2004

Pages:

Including cover page

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# **FACSIMILE COVER SHEET**

# Amrad Corporation Limited

Please find attached information being furnished by Amrad Corporation Limited to the Securities and Exchange Commission.

General Counsel & Company Secretary

Doc# 105059 v1

amrad-#105059-v1-securities\_exchange\_commission\_(sec)\_fax.doc A biotechnology research & development company Page I of I



amrad corporation limited abn 37 006 614 375 576 swan street richmond victoria australia 3121

telephone (61 3) 9208 4000 facsimile (61 3) 9208 4089 http://www.amrad.com,au

22 September 2004

Securities and Exchange Commission Division of Corporate Finance 450 Fifth Street NW WASHINGTON DC 20549 USA

Dear Sirs

AMRAD Corporation Limited Rule 12g3-2(b) Exemption (File No. 82-4867)

The enclosed information is being furnished by AMRAD Corporation Limited ("AMRAD") under paragraph (b)(1)(i) of Rule 12g3-2 under the Securities Exchange Act of 1934 ("the Exchange Act"). AMRAD's file number is indicated in the upper right hand corner of each unbound page and the first page of each bound document furnished herewith.

In accordance with paragraphs (b)(4) and (b)(5) of the Rule, the documents furnished herewith are being furnished with the understanding that such documents will not be deemed "filed" with the Securities and Exchange Commission or otherwise subject to the liabilities of Section 18 of the Exchange Act, and that neither this letter nor the furnishings of such documents shall constitute an admission for any purpose that AMRAD is subject to the Exchange Act.

Yours sincerely

Robyn Fry

General Counsel & Company Secretary

Doc# 106999 v1

# Rule 12g3-2(b) Card Received from the SEC

AMRAO Corporation Linited	FILENO. 82- 4867
9 4 98	

This will advise that the issuer has been added to the list of those foreign private issuers that claim exemption pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Please be further advised that in order to continue to claim this exemption, the issuer must furnish to the Commission, on a timely basis, all information required by Rule 12g3-Z(b). This includes all relevant documents since the date of your initial submission. The burden of furnishing such information rests with the issuer, even if it delegates that responsibility to another, and the staff will look to the issuer for compliance. If the issuer is a member of an affiliated or control group which normally prepares reports, press releases, etc., in a single document, a separate report must be submitted for each issuer that claims an exemption under the rule because separate files are maintained for each issuer.

ALL FUTURE SUBMISSIONS MUST PROMINENTLY INDICATE THE EXEMPTION NUMBER IN THE UPPER RIGHT HAND CORNER OF EACH UNBOUND PAGE AND THE FIRST PAGE OF EACH BOUND DOCUMENT PURSUANT TO THE IDENTIFICATION PROVISIONS OF THE RULE. FAILURE TO SO INDICATE WILL RESULT IN THE SUBMISSION BEING RETURNED TO THE SENDER AND THE SUBMISSION NOT BEING RECORDED, RESULTING IN POSSIBLE LOSS OF THE EXEMPTION.



Australian Stock Exchange Limited ABN 98 008 624 691 Exchange Centre Level 4 , 20 Bridge Street Sydney NSW 2000

PO Box H224 Australia Square NSW 1215

Telephone 61 2 9227 0334

Internet http://www.asx.com.au DX 10427 Stock Exchange Sydney

**FACSIMILE** 

Department: COMPANY ANNOUNCEMENTS OFFICE

DATE:

20/09/2004

TIME:

18:04:41

TO:

AMRAD CORPORATION LIMITED

FAX NO:

03-9208-4356

FROM:

AUSTRALIAN STOCK EXCHANGE LIMITED - Company Announcements Office

SUBJECT:

CONFIRMATION OF RECEIPT AND RELEASE OF ANNOUNCEMENT

## MESSAGE:

We confirm the receipt and release to the market of an announcement regarding:

Proxy Form

#### PLEASE NOTE:

In accordance with Guidance Note 14 of ASX Listing Rules -

- Use of ASX Online for lodgement of company announcements becomes mandatory from 1 July 2003
- · Handwritten and hand-delivered company announcements are no longer accepted
- Fee of A\$38.50 (including GST) applies from <u>1 March 2003</u> for announcements <u>faxed</u> to CAP
- New CAP fax number from 1 March 2003 for announcements sent within Australia is 1900 999 279

# Robyn Fry

From:

Sent:

To:

Subject:

ASX.Online@asx.com.au Monday, 20 September 2004 18:05 rfry@amrad.com.au; nhaw@amrad.com.au AML - ASX Online e-Lodgement - Confirmation of Release



ASX confirms the release to the market of Doc ID: 165222 as follows: Release Time: 20-Sep-2004 18:04:37 ASX Code: AML File Name: 165222.pdf Your Announcement Title: Amrad 2004 AGM proxy form





# **Amrad Corporation Limited**

ABN 37 006 614 375

Mark this box with an 'X' if you have made any changes to your address details (see reverse)

SAMPLE CUSTOMER

# **Proxy Form**

All	correspondence.	44
All	correspondence	m

Computershare Investor Services Pty Limited GPO Box 242 Melbourne Victoria 3001 Australia Enquiries (within Australia) 1300 850 505 (outside Australia) 61 3 9415 4000 Facsimile 61 3 9473 2555 www.computershare.com

SAMPLE ST	REET				Security	older Refer	rence Numbe	r (SRN)	
SAMPLE STI SAMPLETOV	REET	<b>0</b> 0		ļ	AML				
Appointment of Proxy					I 123	34567	890	IND	
I/We being a member/s of Amrad Corporation Limite	ed and entitled to	attend and vote t	ereby appoint						
the Chairman of the Meeting (mark with an 'X')	₹				Write here the nam this person is some Meeting.				-
or tailing the person named, or if no person is name directions (or if no directions have been given, as It 452 Johnston Street, Abbolsford, Victoria on Thursc	e proxy sees fit)	at the Annual Ger	eral Meeting of A	unuad Corporati	on Limited to be held at the Computersha				
below, please place a interest in the outcommark this box, and you	Meeting is you mark in this bo ne of those item ou have not dire	ir nominated pro ix. By marking t s and that votes cled your proxy	his box you ack cast by him, of how to vote, th	nowledge that ther than as pr e Chairman of	efault, and you have not directed you the Chaiman of the Meeting may e; oxy holder, would be disregarded be the Meeting will not cast your votes	cercise your p cause of that on Items 4, 5	proxy even if he interest, if you	has an do not	
of each of these item  Voting directions to your pro	s	, ,	•		. The Chairman of the Meeting inten-	ds to vote un	directed proxies		
of each of these item	s	, ,	•	indicate	-	ds to vote un	directed proxies  Against		
of each of these item Voting directions to your pro	xy - pleas	se mark	X to	indicate	your directions		·	in favour	
of each of these item Voting directions to your pro	xy - pleas	se mark	X to	indicate	your directions  BUSINESS  Approval of Issue of Options		·	in favour	
of each of these item  Voting directions to your pro  ORDINARY BUSINESS  Item 1 Consideration of Reports  Item 2 To re-elect a Director -	xy - pleas	se mark	X to	SPECIAL Item 4	your directions  BUSINESS  Approval of Issue of Options to Chief Executive Officer  Approval of Further Issue of Options to Chief Executive		·	in favour	

PLEASE SIGN HERE This	section must be signed in accordance w	ith the instructions overleaf to enable you	r directions to	be im	plemen
ndividual or Securityholder 1	Securityholder 2	Securityholder 3			
Sole Director and Sole Company Secretary	Director	Director/Compan	y Secretary		
				,	,
				,	•
Contact Name		Contact Daytime Telephone	Date		•

1 f you mark the Abstain box for a particular item, you are directing your proxy not to vote on your behalf on a show of hands or on a poll and your votes will not be counted in



# How to complete this Proxy Form

#### 1 Your Address

This is your address as it appears on the company's share register. If this information is incorrect, please mark the box and make the correction on the form. Securityholders sponsored by a broker (in which case your reference number overleaf will commence with an 'x') should advise your broker of any changes. Please note, you cannot change ownership of your securities using this form.

#### 2 Appointment of a Proxy

If you wish to appoint the Chairman of the Meeting as your proxy, mark the box. If the person you wish to appoint as your proxy is someone other than the Chairman of the Meeting please write the name of that person. If you leave this section blank, or your named proxy does not attend the meeting, the Chairman of the Meeting will be your proxy. A proxy need not be a securityholder of the company.

#### 3 Votes on Items of Business

You may direct your proxy how to vote by placing a mark in one of the boxes opposite each item of business. All your securities will be voted in accordance with such a direction unless you indicate only a portion of voting rights are to be voted on any item by inserting the percentage or number of securities you wish to vote in the appropriate box or boxes. If you do not mark any of the boxes on a given item, your proxy may vote as he or she chooses. If you mark more than one box on an item your vote on that item will be invalid.

#### 4 Appointment of a Second Proxy

You are entitled to appoint up to two persons as proxies to attend the meeting and vote on a poll. If you wish to appoint a second proxy, an additional Proxy Form may be obtained by telephoning the company's share registry or you may copy this form.

To appoint a second proxy you must:

- (a) on each of the first Proxy Form and the second Proxy Form state the percentage of your voting rights or number of securities applicable to that form. If the appointments do not specify the percentage or number of votes that each proxy may exercise, each proxy may exercise half your votes. Fractions of votes will be disregarded.
- return both forms together in the same envelope.

#### 5 Signing Instructions

You must sign this form as follows in the spaces provided:

Individual:

where the holding is in one name, the holder must sign.

Joint Holding:

where the holding is in more than one name, all of the securityholders should sign.

Power of Attorney:

to sign under Power of Attorney, you must have already lodged this document with the registry. If you have not previously lodged this document for notation, please attach a certified photocopy of the Power of Attorney

to this form when you return it.

Companies:

where the company has a Sole Director who is also the Sole Company Secretary, this form must be signed by that person. If the company (pursuant to section 204A of the Corporations Act 2001) does not have a Company Secretary, a Sole Director can also sign alone. Otherwise this form must be signed by a Director jointly with either another Director or a Company Secretary. Please indicate the office held by signing in the appropriate place.

If a representative of the corporation is to attend the meeting the appropriate "Certificate of Appointment of Corporate Representative" should be produced prior to admission. A form of the certificate may be obtained from the company's share registry,

# Lodgement of a Proxy

This Proxy Form (and any Power of Attorney under which it is signed) must be received at an address given below no later than 48 hours before the commencement of the meeting at 11:00am on Thursday 21 October 2004. Any Proxy Form received after that time will not be valid for the scheduled meeting.

Documents may be lodged using the reply paid envelope or:

IN PERSON

Registered Office - 576 Swan Street, Richmond VIC 3121

Share Registry - Computershare Investor Services Pty Limited, Yarra Falls, 452 Johnston Street, Abbotsford VIC 3067

BY MAIL

Registered Office - 576 Swan Street, Richmond VIC 3121

Share Registry - Computershare Investor Services Pty Limited, GPO Box 242, Melbourne VIC 3001 Australia

BY FAX

61 3 9473 2555

007117 V\_008HR18



amrad corporation limited abn 37 006 614 375 576 swan street richmond victoria australia 3121 telephone (61 3) 9208 4000 facsimile (61 3) 9208 4356 http://www.amrad.com.au

To:

The Securities and Exchange Commission

Company:

Fax:

0011 1 202 942 9624

From:

Robyn Fry - Company Secretary

Fax:

(+61 3) 9208 4356

Date:

22 September 2004

Pages:

Ь

Including cover page

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# **FACSIMILE COVER SHEET**

# **Amrad Corporation Limited**

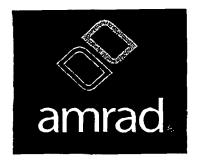
Please find attached information being furnished by Amrad Corporation Limited to the Securities and Exchange Commission.

Robyn Fry

General Counsel & Company Secretary

Doc# 105059 v1

amrad-#105059-v1-securities\_exchange\_commission\_(sec)\_fax.doc A biotechnology research & development company



amrad corporation limited abn 37 006 614 375 576 swan street richmond victoria australia 3121

telephone (61 3) 9208 4000 facsimile (61 3) 9208 4089 http://www.amrad.com.au

22 September 2004

Securities and Exchange Commission Division of Corporate Finance 450 Fifth Street NW WASHINGTON DC 20549 USA

Dear Sirs

AMRAD Corporation Limited Rule 12g3-2(b) Exemption (File No. 82-4867)

The enclosed information is being furnished by AMRAD Corporation Limited ("AMRAD") under paragraph (b)(1)(i) of Rule 12g3-2 under the Securities Exchange Act of 1934 ("the Exchange Act"). AMRAD's file number is indicated in the upper right hand corner of each unbound page and the first page of each bound document furnished herewith.

In accordance with paragraphs (b)(4) and (b)(5) of the Rule, the documents furnished herewith are being furnished with the understanding that such documents will not be deemed "filed" with the Securities and Exchange Commission or otherwise subject to the liabilities of Section 18 of the Exchange Act, and that neither this letter nor the furnishings of such documents shall constitute an admission for any purpose that AMRAD is subject to the Exchange Act.

Yours sincerely

Robyn Fry

General Counsel & Company Secretary

Doc# 106999 v1

# Rule 12g3-2(b) Card Received from the SEC

ISSUER AMRAO	Corporation	Linitod	FILE 82-	4867
9/4/98				

This will advise that the issuer has been added to the list of those foreign private issuers that claim exemption pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Please be further advised that in order to continue to claim this exemption, the issuer must furnish to the Commission, on a timely basis, all information required by Rule 12g3-2(b). This includes all relevant documents since the date of your initial submission. The burden of furnishing such information rests with the issuer, even if it delegates that responsibility to another, and the staff will look to the issuer for compliance. If the issuer is a member of an affiliated or control group which normally prepares reports, press releases, etc., in a single document, a separate report must be submitted for each issuer that claims an exemption under the rule because separate files are maintained for each issuer.

ALL FUTURE SUBMISSIONS MUST PROMINENTLY INDICATE THE EXEMPTION NUMBER IN THE UPPER RIGHT HAND CORNER OF EACH UNBOUND PAGE AND THE FIRST PAGE OF EACH BOUND DOCUMENT PURSUANT TO THE IDENTIFICATION PROYISIONS OF THE RULE. FAILURE TO SO INDICATE WILL RESULT IN THE SUBMISSION BEING RETURNED TO THE SENDER AND THE SUBMISSION NOT BEING RECORDED, RESULTING IN POSSIBLE LOSS OF THE EXEMPTION.



Australian Stock Exchange Limited ABN 98 008 624 691 Exchange Centre Level 4, 20 Bridge Street Sydney NSW 2000

PO Box H224 Australia Square NSW 1215

Telephone 61 2 9227 0334

Internet http://www.asx.com.au DX 10427 Stock Exchange Sydney

FACSIMILE

Department: COMPANY ANNOUNCEMENTS OFFICE

DATE:

20/09/2004

TIME:

18:05:51

TO:

AMRAD CORPORATION LIMITED

FAX NO:

03-9208-4356

FROM:

AUSTRALIAN STOCK EXCHANGE LIMITED - Company Announcements Office

SUBJECT:

CONFIRMATION OF RECEIPT AND RELEASE OF ANNOUNCEMENT

## MESSAGE:

We confirm the receipt and release to the market of an announcement regarding:

Amrad Seeks Shareholder Approval for CEO Options

# PLEASE NOTE:

In accordance with Guidance Note 14 of ASX Listing Rules -

- Use of ASX Online for lodgement of company announcements becomes mandatory from 1 July 2003
- Handwritten and hand-delivered company announcements are no longer accepted
- Fee of A\$38.50 (including GST) applies from <u>1 March 2003</u> for announcements <u>faxed</u> to CAP
- New CAP fax number from <u>1 March 2003</u> for announcements sent within Australia is 1900 999 279



# Robyn Fry

From:

ASX.Online@asx.com.au

Sent:

Monday, 20 September 2004 18:06

To:

Subject:

rfry@amrad.com.au; nhaw@amrad.com.au AML - ASX Online e-Lodgement - Confirmation of Release



165223.pdf (90 KB)

ASX confirms the release to the market of Doc ID: 165223 as follows: Release Time: 20-Sep-2004 18:05:48 ASX Code: AML File Name: 165223.pdf Your Announcement Title: Amrad seeks shareholder approval for CEO options



amrad corporation limited abn 37 006 614 375 576 swan street richmond victoria australia 3121 telephone (61 3) 9208 4320 facsimile (61 3) 9208 4352 http://www.amrad.com.au

Monday 20 September 2004

# AMRAD SEEKS SHAREHOLDER APPROVAL FOR CEO OPTIONS

Amrad Corporation Limited (ASX:AML) today reported the Board decision to vary the exercise price of 400,000 options proposed to be issued to the Chief Executive Officer, Dr Pete Smith, subject to shareholder approval at the Company's Annual General Meeting to be held on 21 October 2004.

The terms of the exercise price for Dr Smith's options originally proposed by the Board are detailed in the explanatory notes to the 2004 Annual General Meeting Notice that has been despatched to shareholders.

The exercise price proposed by the Board for Dr Smith's options will now be increased following submissions by Dr Smith that the terms of his options should not be more advantageous than those currently applying to other Company employee options. The Board will therefore now seek shareholder approval to issue options to Dr Smith at the increased exercise price of \$1.15 (to be adjusted in accordance with ASX guidelines as a result of the Avexa demerger). The options will, as set out in the explanatory notes, vest at the time of issue and will be exercisable within five years of the issue date.

The amount of the adjustment per option will be calculated in accordance with the formula prescribed in the Company's Information Memorandum on the basis of an apportionment between the actual market values of Amrad shares and Avexa shares over the first five ASX trading days of the Avexa shares.

Commenting on the Board decision to vary the CEO options exercise price the Chairman, Mr Bob Moses said the Board was delighted with Dr Smith's strong performance in the Chief Executive Officer role over the past financial year.

"Drawing on his in-depth industry knowledge, Dr Smith has laid a new strategic foundation which is rapidly transforming Amrad into a much more focussed company. I am very confident this strategic focus, together with implementation of more robust operating disciplines, will greatly enhance value-creation for shareholders. The corporate performance targets initially established for Pete as part of his remuneration arrangements have been satisfied and in many respects he has exceeded the Board's expectations," Mr Moses said.

For further information contact:

Dr Pete Smith
Chief Executive Officer

Telephone: 61 3 9208 4108

For additional company information refer to Amrad's website: www.amrad.com.au

Doc# 122636 v2

A biotechnology research & development company

Page 1 of 1



amrad corporation limited abn 37 006 614 375 576 swan street richmond victoria australia 3121 telephone (61 3) 9208 4000 facsimile (61 3) 9208 4356 http://www.amrad.com.au

To:

The Securities and Exchange Commission

Company:

Fax:

0011 1 202 942 9624

From:

Robyn Fry - Company Secretary

Fax:

(+61 3) 9208 4356

Date:

22 September 2004

Pages:

53

Including cover page

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# **FACSIMILE COVER SHEET**

# **Amrad Corporation Limited**

Please find attached information being furnished by Amrad Corporation Limited to the Securities and Exchange Commission.

P Robyn Fry

General Counsel & Company Secretary

Doc# 105059 v1

amrad#105059-v1-securities\_exchange\_commission\_(sec)\_fax.doc
A biotechnology research & development company Page 1 of 1



amrad corporation limited abn 37 006 614 375 576 swan street richmond victoria australia 3121

telephone (61 3) 9208 4000 facsimile (61 3) 9208 4089 http://www.amrad.com.au

22 September 2004

Securities and Exchange Commission
Division of Corporate Finance
450 Fifth Street NW
WASHINGTON DC 20549
USA

Dear Sirs

AMRAD Corporation Limited Rule 12g3-2(b) Exemption (File No. 82-4867)

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Yours sincerely

(J

Robyn Fry General Counsel & Company Secretary

Doc# 106999 v1

OΤ

# Rule 12g3-2(b) Card Received from the SEC

ISSUER AMRAO	Corporation Limited	FILE NO. B2- 4867
9/4/98		

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Australian Stock Exchange Limited ABN 98 008 624 691 Exchange Centre Level 4, 20 Bridge Street Sydney NSW 2000

PO Box H224 Australia Square NSW 1215

Telephone 61 2 9227 0334

Internet http://www.asx.com.au DX 10427 Stock Exchange Sydney

**FACSIMILE** 

Department: COMPANY ANNOUNCEMENTS OFFICE

DATE:

20/09/2004

TIME:

18:03:58

TO:

AMRAD CORPORATION LIMITED

FAX NO:

03-9208-4356

FROM:

AUSTRALIAN STOCK EXCHANGE LIMITED - Company Announcements Office

SUBJECT:

CONFIRMATION OF RECEIPT AND RELEASE OF ANNOUNCEMENT

## MESSAGE:

We confirm the receipt and release to the market of an announcement regarding:

Annual Report 2004

### PLEASE NOTE:

In accordance with Guidance Note 14 of ASX Listing Rules -

OΤ

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- New CAP fax number from 1 March 2003 for announcements sent within Australia is 1900 999 279



# Robyn Fry

From:

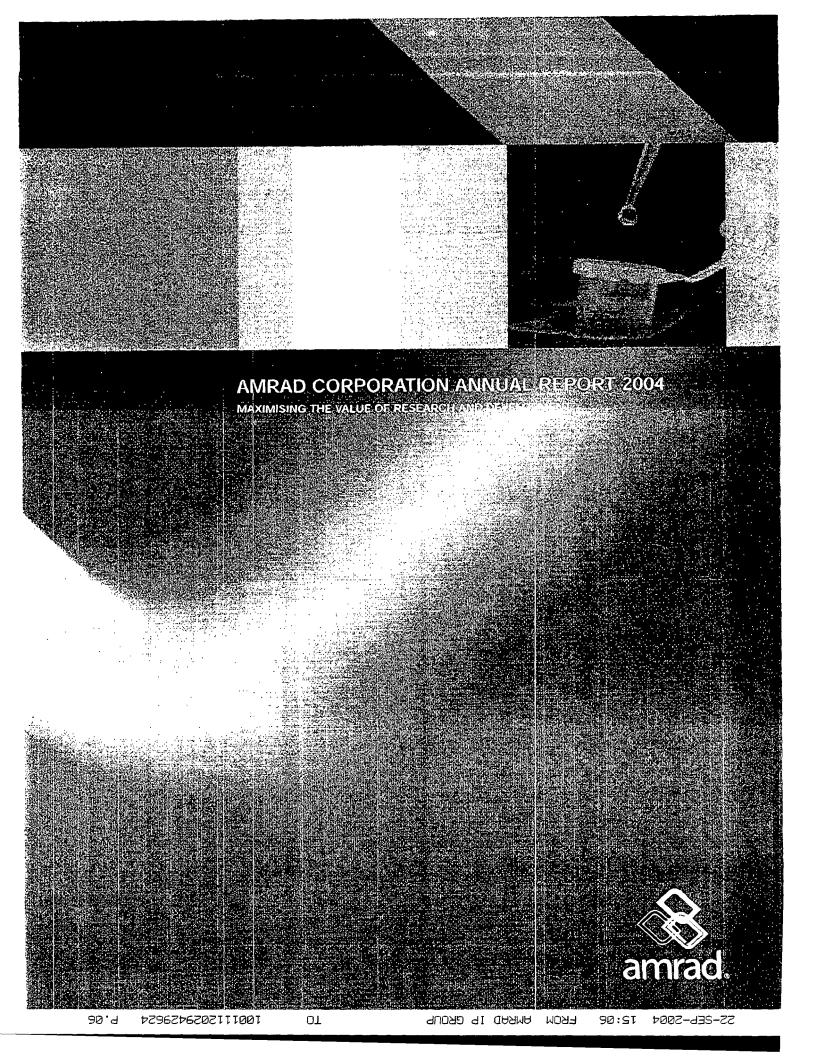
ASX.Online@asx.com.au

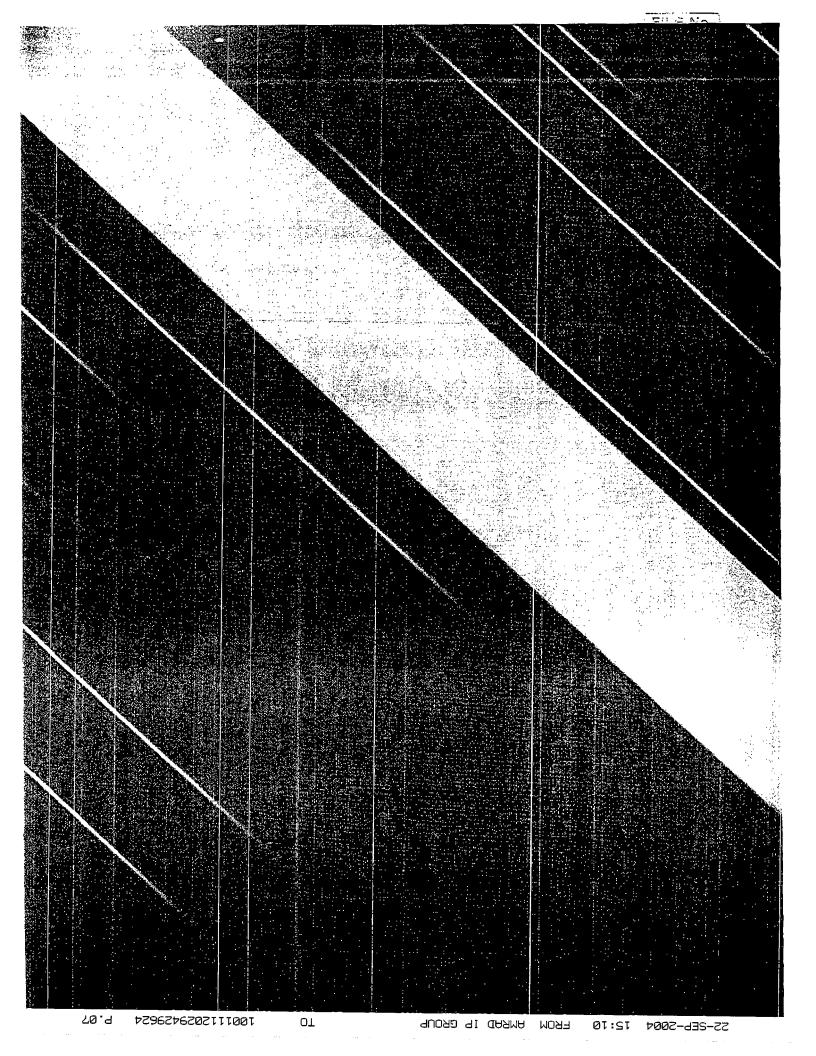
Sent:

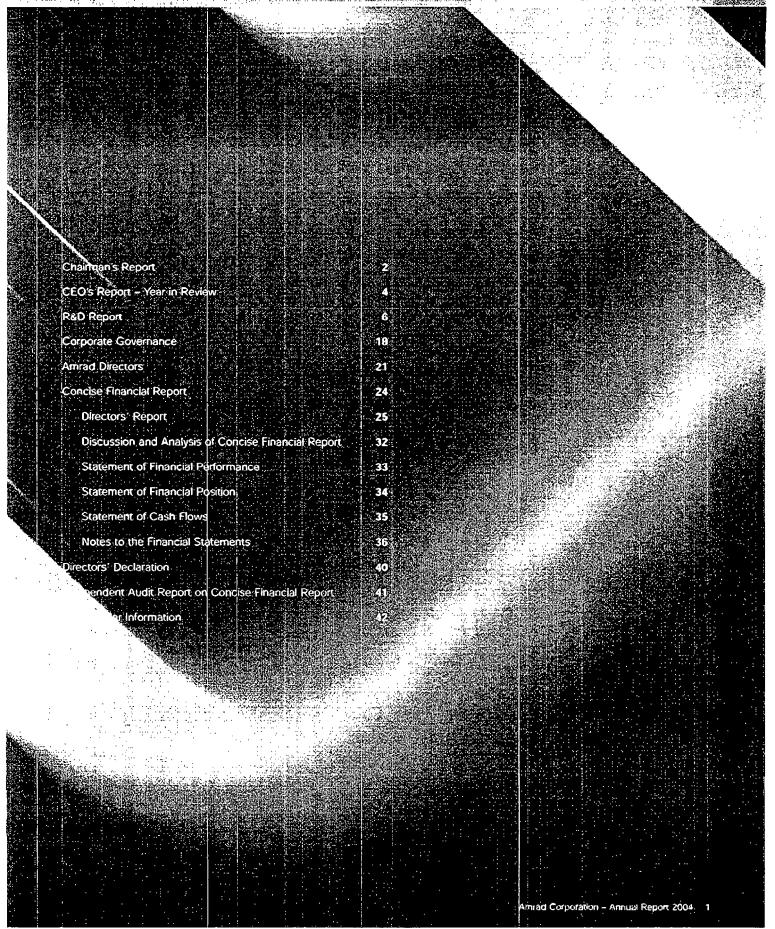
To: Subject: Monday, 20 September 2004 18:04
rfry@amrad.com.au; nhaw@amrad.com.au
AML - ASX Online e-Lodgement - Confirmation of Release



ASX confirms the release to the market of Doc ID: 165220 as follows: Release Time: 20-Sep-2004 18:03:54 ASX Code: AML File Name: 165220.pdf Your Announcement Title: Amrad 2004 Annual Report



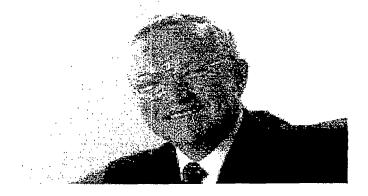




OΤ

12:15

# CHAIRMAN'S REPORT



It is pleasing to report that the strategies announced at the October 2003 AGM are being implemented on time, on budget and according to plan. The corporate strategy is to transform Amrad into a biotechnology company which has a clear focus on research and development of biologicals with a specific emphasis on cytokines aimed at cancer targets, cardiovascular diseases and diseases involving severe and debilitating inflammation such as rheumatoid arthritis and asthma.

This strategy builds on Amrad's core technical capabilities and its strong intellectual property portfolio, and provides a well-defined development structure for efficient progression of promising research projects which Amrad is developing in collaboration with world class research institutions such as the Walter and Eliza Hall Institute (WEHI), and commercial partners including Merck & Co., and Cambridge Aritibody Technologies.

At the 2003 AGM we also announced plans to spiri out Amrad's promising portfolio of anti-viral projects into a newly created, stand-alone company. This company, Avexa, is now a separate legal entity with initial working capital of \$12 million. Subject to shareholder and court approval, Avexa will become a listed company with existing Amrad shareholders owning 80.01 per cent of the Avexa shares and Amrad itself holding the remaining 19.99 per cent of Avexa shares. Key research and administrative stall who have been associated with the portfolio of anti-viral projects have become employees of Avexa. Facilities, services and infrastructure continue to be provided by Amrad to Avexa on 'arms-length' commercial terms so that Avexa is immediately a fully operational company, able to continue uninterrupted the development of its exciting portfolio of anti-viral products.

A comprehensive Information Memorandum explaining details of the Avexa demerger has been mailed to all Amrad shareholders. Subsequently, Dr Hugh Niall has been appointed Chairman of Avexa and Dr Julian Chick has been appointed Avexa's Chief Executive Officer and Executive Director.

The strategic reasons for creating Avexa are to not only create shareholder value, but to ensure capital market recognition of that value. The Amrad Board of Directors has for some time been concerned that whilst both the biologicals project portfolio and the anti-viral project portfolio remain within Amrad, shareholders, and the capital markets generally, would continue to have significant difficulty understanding and attributing appropriate value to the totality of Amrad's research and development activities.

The Board believes the Amrad share price tends to reflect the value attached to only two or perhaps three of the Company's biological projects, leaving little or no value attributed to the anti-viral projects. In addition, the Board recognises that biological research and development is in many important respects, very different from anti-viral research and development – the scientific skills are different, the facilities and infrastructure are different, the clinical and regulatory process is different, and the timeframe and risks along the path to commercialisation are different. Creating Avexa is a very positive way to address all of these issues and we believe gives Amrad/Avexa shareholders the best opportunity to realise full value of both technology portfolios.

#### Performance Review

Amrad's financial results for the year might best be described as 'mixed fortunes'. On the positive side of the ledger, milestone payments received from the license of IL-13R to Merck & Co., added AUD\$8.1 million to revenues; however, we were disappointed by the failure of the Emfilermin Phase II clinical trial Serono SA conducted under license from Amrad. We had expected this license to yield a significant milestone payment.

Net revenues for the year were \$16.4 million; net operating expenses were \$18.7 million with a further \$1.8 million of non-recurring expenditure, thereby generating a net operating loss of \$3.5 million. Cash and financial assets available at 1 July 2003 were preserved such that year end cash reserves remained at \$60.0 million, of which \$12 million has been invested in Avexa subsequent to reporting date.

Forward estimates of financial performance in biotechnology are always challenging, but during the current year ending 30 June 2005, we do expect to receive additional revenue from the licence with Merck. Operating expenses will reduce significantly as a result of both structural refinements and the spinout of Avexaleaving the prospect of only a modest consumption of cash and a healthy cash position at year end.

Amrad will consider the resumption of the on market share buy-back program after the ASX listing of Avexa whereby up to 10.9 million shares remain able to be purchased and cancelled before 5 April 2005.

At the AGM last October I was pleased to accept the position as Chairman of the Company; and particularly grateful to Mr Olal O'Duill, for his contribution to the Company which I personally value highly and which has greatly facilitated a smooth transition and efficient implementation of the corporate strategy.

The 2003 AGM was also the date Dr Peter Smith joined Amrad as its Chief Executive. I am pleased to report that Pete has already brought great value to the Company, particularly in providing leadership and articulating a clear vision for the future growth and development of the Company. Pete brings to Amrad the ideal mix of relevant scientific knowledge and intimate understanding of the commercial world of biotechnology. Pete's highly developed network of key individuals internationally is having a significant impact in elevating awareness and enhancing the credibility of Amrad in Northern Hemisphere capital markets as well as in Australia.

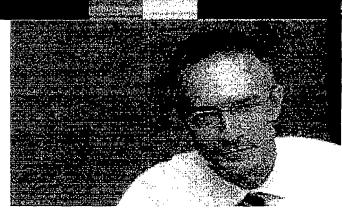
An important objective of the Board over the next one to three years is to strengthen the Company's share register through encouragement of long term institutional investments, including participation of international investors with experience in the biotech sector as well as local institutional investors. Shareholders' valuation of good quality biotechnology stocks listed on the ASX has consistently resulted in share prices which are an order of magnitude lower than comparable biotech stocks in North America and Europe. I believe this is the case with the Amrad share price. Accordingly, in addition to his responsibility for the day-to-day operation of Amrad. Pele and his management team will be promulgating the Armrad story to shareholders and potential shareholders in key North American and European capital markets as well as in Australia during the coming year. Although no decision is imminent, consideration will also be given to mechanisms which enhance liquidity and facilitate international investment.

In summary, I believe the future of both Amrad and Avexa is extremely exciting and holds promise of substantial financial rewards for those who retain their shareholdings in both companies as long term investments. During the year I expect both companies to make good progress with their respective flagship research projects. Fach company has projects that could reach a point where the company is in a position to announce major outcomes which, if positive, would greatly enhance the underlying value of their respective shares. I am every bit as optimistic about Avexa's future as I am about the future of Amrad.

Mr Robert W Moses Chairman

FROM

# CEO'S REPORT - YEAR IN REVIEW



The past 12 months has been another period of charge for Amrad after which the Company is emerging with a much clearer identity and focus. In some respects these recent changes represent the continuation of a process that started many years ago. Amrad was established to assist Australian institutes commercialise their technologies and, as a result, its portfolio was diverse; reflecting the research interests of those institutes. Amrad also has had business interests in diagnostics, pharmaceutical sales; and natural products screening and chemistry which was spun out as ExGenix Limited (now Cerylid Biosciences Limited) in January 2000.

To be really successful, however, a biotechnology company must be a recognisable leader in its area of expertise and must build on that position in order to remain competitive. Over the years Amrad has developed key capabilities and it is around these that the Board believes future value can be created. The strategic plan that was unveiled at the AGM last year has been put into effect, resulting in the creation of two companies: Avexa, focussed on small-molecule drugs for the treatment of viral and bacterial infections; and Amrad which is using protein-based approaches to the treatment of inflammation and cancer. Both companies now have the right platforms on which to build their businesses, based on well-defined and, importantly, more comprehensible business strategies.

This has been a process of evolution for Amrad and Avexa and both companies now have business models aligned with those that have proven successful in the industry.

## Highlights of the Year

- Two US\$3 million milestone payments were received from Merck as part of our agreement in the field of asthma therapies. The IL-13R antagonist project has a very high priority within Merck and these milestones are not only important financially to Amrad but also provide an indication of the rapid progress. that has been made and the delivery on key objectives by the teams here and at Merck, IL-13 has emerged as one of the most exciting targets in the field of asthma research, being directly implicated in practically every facet of the disease. The market potential of a breakthrough treatment for asthmawould be very large; hospitalizations of asthmatics ineffectively controlled by current medications cost around U5\$13 billion in the United States alone.

- Our collaboration with Cambridge Antibody Technology (CAT) has resulted in the production of a highly potent, fully-human, antibody against the GM-CSF receptor. This lead antibody will soon enter formal pro-clinical testing as a preface to its first administration in man. We will share the costs of clinical development and the revenues from any future licensing deals equally with CAT. Models of the disease suggest that GM-CSF receptor antagonists could be more effective than currently available products in managing the symptoms and joint destruction seen in rheumatoid arthriús.
- The growth of new blood vessels is involved in numerous. normal processes such as growth and wound healing. This process, called angiogenesis, is also involved in disease processes such as cancer and rheumatoid arthritis. Amrad has rights to one of the molecules that stirnulates angiogenesis. VEGF-B as well as inhibitors thereof. Amrad's scientists have developed antibodies that inhibit VEGF-B and these are being evaluated in collaboration with scientists at the Peter MacCallum Cancer Institute and the Queensland Institute for Medical Research to understand its role in cancer and rheumatoid arthritis respectively. Results from these studies are expected in the year ahead. The field of angiogenesis is generating considerable excitement amongst scientists and clinicians following the successful clinical trials of Genentech's drug Avastin," an antibody against VEGF-A. Those results added tens of billions of dollars to Genentech's market capitalisation.
- On a negative note, the phase II clinical trial of emfilermin. (leukaemia inhibitory factor - LIF) in couples who had failed to have a baby after previous cycles of infertility treatment, did not demonstrate superiority compared with placebo. This trial refuted the positive results seen in an earlier clinical trial and Amrad and its licensee Serono will no longer pursue this indication.
- As mentioned above, the decision to spin out Amrad's anti-infectives programs into a separate company, Avexa, has been put into effect. Avexa is developing innovative small-molecule drugs for the treatment of serious infections. such as human immunodeficiency virus (HIV), hepatitis B virus (HBV) and antibiotic resistant bacteria or 'superbugs'. Avexa has sufficient cash resources to reach important value creating preclinical studies in each of its programs. With a clear identity

and a dedicated management team it will be easier for Avexa to communicate its story and build its business. The discovery and development of small molecule drugs, the mainstay of the 'traditional' pharmaceutical industry, is very different to the technologies that Amrad is employing in its programs.

 In March this year Amrad held its first R&D Day for analysts. and fund managers. This provided an excellent forum to go into more detail about the science and, importantly, the market opportunities for the products that we are developing. We intend to repeat this event annually as a component of a heightened effort to communicate the potential of Amrad's programs.

the Co-operative Research Centre for Cellular Growth Factors (CRC-CGF), a consortium of a number of Australia's most prestigious academic institutions and Amrad, completed its 13 year Mespan in June this year. This CRC has been particularly fruitful and has resulted in Amrad working closely with some of the world's top scientists in the field. Several of Amrad's most important programs have emanated from this collaborative effort including; IL-13R antagonists for asthma; GM-CSFR antagonists for inflammatory diseases; and the SOCS family of proteins. Amrad would like to thank all of those people who helped to make this CRC so fruitful. We are continuing to collaborate with a number of the groups to ensure that the good working relationships are enjoyed beyond the end of the CRC. Amrad has also stated its desire to participate in the proposed CRC for Innovative Drug Discovery which intends to use state-of-theart high throughput screening methods to look for small-molecule drugs against a number of Amrad's targets.

Through efficient use of our cash and through the income received from our licensees Amrad's cash position remained at a very healthy \$60.0 million, in line with our expectations. Whilst we anticipate that our cash 'burn' will remain modest for the coming twelve months, the costs of our programs will inevitably increase beyond that time frame as we enter the crucial clinical stages in their development.

Drug development is a high risk business and those risks are rewarded by the huge sales potential of products that clear all of the regulatory hurdles and demonstrate their safety and utility in the management of disease. Each of Amrad's programs has the chance of making a real difference to individuals suffering

from conditions such as severe asthma, rheumatoid arthritis and cancer. Not only are all of Amrad's programs targeting major diseases, they are all built on the same core capabilities in terms of the science and technology, and these capabilities will help us to skew the odds in our favour. The same is true of Avexa where the expertise of its team in the area of antiviral drug discovery and development may yield new treatments for HIV. hepatitis B and other serious infections.

In closing I must salute the entire team at Amrad which has maintained its focus and dedication during a period of change. The Company's people and their capabilities provide a strong foundation for future success.

Pete Smith

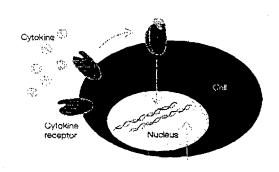
Chief Executive Officer

Amrad is a biopharmaceutical company whose business is the discovery and development of novel, commercially valuable medicines that relieve the suffering of people with inadequately troated diseases.

Amrad's biologicals project portiolio focuses on cytokine biology. Cytokines are messenger proteins that are used by colls within the body to communicate with each other - they interact with specific receptors on the target cell surface and trigger a series of signalling events within the cell that ultimately load to the production of new proteins and the regulation of key physiological processes. Recombinant cytokines produced using DNA technology are currently used to treat a variety of diseases including anemia, multiple sclerosis and hepatitis.

Unfortunately, if cytokines are produced at an inappropriate site or in excessive quantities, the consequences can be severe. For example, chronic inflammatory diseases such as rheumatoid arthritis (RA) and asthma are known to result from inappropriate cytokine action. Novel therapeutics designed to block the activity of selected cytokines are now available for the treatment of RA and are also being investigated for a variety of other common inflammatory diseases.

Through its network of collaborators Amrad has been involved in the discovery of a number of cytokines and cytokine receptors. that regulate key physiological processes or are involved in the development of significant diseases. Amrad has the intellectual property rights pertaining to these discoveries and, based on this position, is currently pursuing the development of new cytokine-based therapeutics with the potential to treat chronic inflammatory diseases and cancer.



- Growth and development
- Fight infection
- New blood cells

The following is an overview of Amrad's primary cytokine biology research and development programs.

Project: IL-13R alpha 1 Antibody

A new approach to treating asthma

## SNAPSHOT

Description:

Product type: Indication:

Research collaborator:

Commercial partner: Development status: Next project milestone:

Patents status:

Interleukin -13 receptor alpha1 .

(IL-13Ra1) antagonist Monoclonal antibody

Asthma

Cooperative Research Centre for Cellular Growth Factors\*/Walter and Eliza Hall Institute of Medical Research

Merck & Co., Inc. Lead optimisation

Commence preclinical studies Granted in Australia. Pending in Canada, Europe, Japan and the US.

The Cooperative Research Centre for Collular Growth Factors term expired at the end of June 2004.

Asthma is one of the most common diseases in the world. affecting all age and socio-economic groups. Although prevalence varies greatly from country to country, approximately 300 million people suffer from asthma worldwide. In recent years, dospite the development of improved therapeutic agents, the death rate due to asthma has continued to increase in some countries.

Asthma is a condition characterised by reversible airflow limitation and excessive responsiveness of the lung to irritants and stimulants. The exact cause of the disease is poorly understood. however, it is regarded as a disease of chronic inflammation that leads to wheezing, breathlessness, chest tightness and coughing.

Asthma is predominantly treated with two classes of drugs -B agonists, which limit the narrowing of the airways, and inhaled corticosteroids, a class of drugs with anti-inflammatory effects as well as significant and extensive side effects at high doses. In addition, a newer group of compounds, the leukotriene inhibitors, which antagonise the inflammatory response at its final stages, have recently been introduced.

#### Therapeutic Potential

For many patients, adequate control of their asthma is achieved with B agonists and inhaled corticosteroids. However, despite treatment, around 6-10 per cent of asthma patients continue to suffer severe asthma which substantially impacts on their quality of life and is a significant cause of morbidity and mortality. Treatment options are limited for these patients and there exists a substantial need for improved therapeutic agents.

In recent years it has become increasingly apparent that a complex cascade of cytokines contributes to the initiation and maintenance of chronic inflammation. In particular, the cytokine IL-13 has been implicated as having a pivotal role in causing asthma inflammation. The development of drugs to reduce the effects of IL-13 in the lung is an exciting new approach which offers considerable

promise as a novel treatment for asthma. Amrad, together with Merck, is developing therapeutic monoclonal antibodies that target the IL-13Ra1 and that block or inhibit IL-13 activity.

## Commercial Strategy

The IL-13Ra1 project is partnered with Merck and Amrad is working with Merck to develop candidate therapeutic monoclonal antibodies. Merck is responsible for all clinical development and

Amrad received US\$5 million on signing the agreement with Merck in June 2003 and two US\$3 million milestone payments, one in November 2003 and the second in March 2004. The deal is potentially worth US\$112 million plus royalties.

### Project Status

The Amrad/Merck IL-13Ra1 project is in the lead optimisation phase. IL-13Ra1 has been validated as a therapeutic target in asthma. Therapeutic monoclonal antibodies have been generated and are currently being optimised.

## Scientific Rationale

IL-13Rα1 is a shared receptor component for the cytokines IL-13 and IL-4, both of which are important mediators of airway diseases such as asthma. Although many cytokines appear to play a role in the development and progression of asthma, recent studies in mouse models suggest a central and non-redundant role for IL 13. In animal models, IL-13 is a key mediator of the antibody production, inflammatory response, airway reactivity and mucus production, all of which underlie the cause of asthma symptoms.

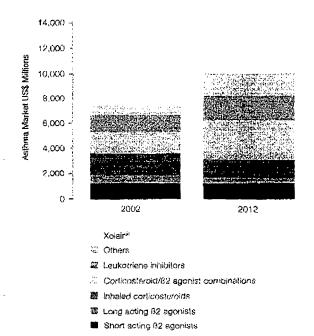
IL-13Rα1 is believed to also play a role in human asthma, as the expression of this receptor has been detected on a variety of cells implicated in the development and maintenance of asthma. As a cell surface molecule essential for IL-13 activity (and at least a proportion of IL-4 activity) the IL-13Ra1 represents a novel and exciting target ideally suited to large molecule based drugs such as human or humanised monoclonal antibodies.

#### CURRENT MARKET AND COMPETITORS

The asthma patient population is typically segmented according to disease severity. An IL-13Ra1 antibody is expected to initially target patients suffering from severe persistent asthma, a patient group currently not adequately managed with existing drugs. Severe persistent asthmatics represent approximately 10 per cent of all asthmatics, and there thus remains significant market potential for new drugs to treat this patient sub-population.

In 2002, the total market for drugs to treat asthma was US\$7 billion and the asthma drug market is expected to grow. to approximately US\$13 billion by 2012, this growth in large part is driven by the launch of new biological treatments. For example, the antibody Xolair® was approved in June 2003 for the treatment of moderate to severe allergic asthma in patients whose symptoms are inadequately controlled by inhaled controlsteroids. Despite its limited target patient population, Xolair is expected to achieve sales of US\$3,3 billion by 2012, representing around 25 per cent of the total asthma market. An IL-13Ron antibody should treat both the allergic and non-allergic forms of asthma and therefore has the potential to target a larger patient population than Xolair.

#### MARKET FOR DRUGS TO TREAT ASTHMA



Source: Nature Reviews Drug Discovery, Volume 3, March 2004 pages 199-200.

## Project: GM-CSFR Antibody

A new treatment for Rhoumatoid Arthritis

#### SNAPSHOT

Description:

Product type: Indication:

Research collaborator:

Commercial partner: Current development status: Next project milestone:

Patent status: ...

Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF) receptor antagonist

Monoclonal antibody Rheumatoid arthritis Cooperative Research Centre

for Cellular Growth Factors"/Walter and Eliza Hall Institute of Medical Research Cambridge Antibody Technology

Lead characterisation Lead candidate enters formal preclinical studies Granted in Australia, Europe. Japan and the US. Pending

\* The Cooperative Research Centre for Cellular Growth Factors term expired at the end of June 2004.

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in Canada.

Rheumatoid Arthritis (RA) is a chronic inflammatory disease of the joints, affecting approximately one per cent of the population in the industrialised world. The disease is two to three times more common in women than in men and can start at any age. with a peak incidence between 40-60 years of age, RA is characterised by overgrowth and inflammation of the membranes within limb joints, and progressive destruction of the surrounding bone and joint surface cartilage. RA commonly leads to significant disability and a substantial reduction in both quality of life and life expectancy if untreated.

RA is characterised by an immune response against a target antigen (as yet unknown) which triggers a cascade of inflammatory changes within the joint. This inflammatory cascade involves a variety of inflammatory cells and is mediated by a number of cytokines, such as interleukin-1 (IL-1), tumour necrosis factor (TNF) and also GM-CSF, the focus of Amrad's drug discovery and development.

## Therapeutic Potential

In recent times, non-specific disease modifying anti-rheumatoid drugs (DMARDs) such as methotrexate which act to suppress cell growth and reduce the rate of joint destruction have been the mainstay of RA treatment. Over the past few years, the approval of biological drugs targeting inflammatory cytokines has led to a revolution in the management of RA.

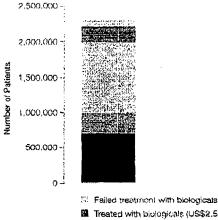
Biological drugs, such as Eribrel®, Remicade® and Humira®, all of which target the cytokine TNF, have greatly improved the therapeutic benefit experienced by RA patients. While a groundbreaking treatment for some, there remains a need for alternative therapeutics. Targeting inflammatory cytokines other than TNF, for example GM-CSF, offers significant potential.

## CURRENT MARKET AND COMPETITORS

Biological drugs were used to treat 231,000 RA patients in the US during 2003, generating sales of approximately US\$2.5 billion. ING Bank has independently forecast that biological drugs will enjoy a 19 per cent annual market growth from 2003 to 2008 to reach an estimated US\$5.7 billion in global annual sales by 2008.

Although anti-TNF therapies such as Enbrel® and Humira® currently dominate the biological drugs market for RA, 32 per cent of patients treated with these therapies fail to respond and a further 26 per cent do not achieve greater than a 50 per cent reduction in symptoms. Therefore, a significant percentage of RA patients receive inadequate treatment - opening up a clear market segment for drugs targeting alternative inflammatory pathways, such as the GM-CSF pathway. pathway.

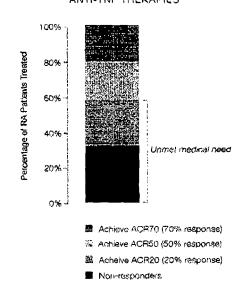
#### BREAKDOWN OF RA MARKET IN US (2003)



- Treated with biologicals (US\$2.5 billion in sales)
- Treated with DMARDs (USS3,6 billion in sales)
- Treated with non-DMARDs
- Not seeking treatment

Source: Smith Barriey Citigroup (2003).

### LONG-TERM RESPONSE RATES TO ANTI-THE THERAPIES



Source: Eshman Brothers (2003).

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## Commercial Strategy

Amrad's partner for the GM-CSF receptor antibody project is the UK-based biotechnology company, Cambridge Antibody fechnology (CAT). The project is partnered on a 50/50 cost share basis. Under the terms of the collaboration Amrad and CAT intend to co-develop a GM-CSF receptor antibody until the end of Phase II clinical trials.

### Project Status

Excellent progress has been made with the generation and selection of lead antibodies. Analysis in appropriate preclinical models has been initiated.

#### Scientific Rationale

The biological activities of GM-CSF indicate that it plays an important role in inflammation and autoimmunity. Recent studies in a variety of mouse models support a central and non-redundant role for GM-CSF in the development and progression of RA. In particular, administration of antibodies to GM-CSF significantly reduces arthritis severity in mouse models of RA.

Project: VEGF-B Antagonist

Novel approach to treating cancer

## **SNAPSHOT**

Vascular Endothelial Growth Factor B Description:

(VEGF-B) antagonist Product type: Monoclonal antibody Indication: Cancer

Research collaborator: Queensland Institute of Medical

Research/ Ludwig Institute for

Cancer Research

Commercial-partner: N/A Development status:

Next project milestone: Patents status:

Lead selection/optimisation Commence preclinical studies Granted in Australia, Canada, Europe and the US. Pending in Japan and

other countries.

Cancer, one of the world's biggest killers, has typically been treated with a broad range of chemotherapies, however there is still a very large unmet clinical need and novel approaches to treating cancer continue to be explored. Solid tumours are dependent on the development of blood vessels (angiogenesis) for the supply of oxygen and nutrients, and inhibiting the growth of new blood vessels is an exciting new approach to the treatment of cancer.

## Therapeutic Potential

VEGF-8, a cytokine produced by the body, stimulates the formation of new blood vessels. This role in vessel formation suggests that inhibiting the effects of VEGF-B may represent an appealing new approach to limiting the blood supply essential for cancer growth.

The first drug in the new anti-angiogenesis class, Genetech's Avastin®, has been approved for use in cancer of the colon and rectum in combination with a conventional anti-cancer drug. An antibody against VEGF-B may broaden the options available in this new therapeutic class, potentially treating tumours not currently targeted by Avastin\*.

A strategy for preventing the formation of blood vessels that support tumour growth is likely to be complementary to more conventional anti-cancer treatments that are typically largeted towards destroying individual cancer cells.

## CURRENT MARKET AND COMPETITORS

In the US there are approximately 1.4 million newly diagnosed cancer cases every year and over nine million people in the US have cancer. The cancer market in the US alone is worth over US\$20 billion per year in drugs sales.

Recently, biological drugs - molecules that are able to target cancer cells and activate one or more killing mechanisms - have entered the cancer market. An example of an anti-cancer biological orug is Rituxan®, an antibody targeting a molecule on B-cell lymphoma and non-Hodgkin's lymphoma. In 2003, Rituxan® (MabThera®) became the number one selling anti-cancer drug worldwide, with estimated sales for 2004 of US\$3.1 billion. expected; to rise to US\$4.4 billion by 2008.

The recent FDA approval of Genentech's Avastin®, a specific anti-angiogenic monoclonal antibody for colorectal cancer, has also raised interest in the potential for other anti-angiogenesis drugs. Current estimates for 2005 sales of Avastin® are around US\$850 million, with the price around US\$4,400 per patient per month.

#### Commercial Strategy

Amrad is currently working with its research collaborators to identify and validate a lead antibody candidate. Amrad's commercial strategy is to continue to develop VEGI-B antagonists internally, adding value to the project before seeking a potential partner for the project. Amrad and the Ludwig Institute for Cancer Research have a cross-licensing agreement for their respective VEGF-B patents and share any commercial benefits received by either party.

#### Project Status

VEGF-B antibodies are currently being assessed as potential therapeutic agents in animal models of cancer.

### Scientific Rationale

The VEGF family of related cytokines has five members, VEGF-A, B, C, D and PIGF, all of which have been shown to play some role in the differentiation, recruitment, proliferation and/or survival of endothelial cells. In vivo, these activities represent key events in angiogenesis.

The role of VEGF-A in the blood vessel formation required for the growth and metastasis of solid tumours has been well documented in a variety of animal models. Clinical data from cancer patients and the recent FDA approval of Avastin®, has

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provided validation of the inhibition of blood vessel formation as an effective approach to cancer therapy. There is now a significant body of published data also supporting a role for VEGF-B in blood vessel formation and a monoclonal antibody-based VEGF-B antagonist may similarly inhibit this process.

Project: VEGF-B Gene and Protein Therapies Repairing damaged hearts

## SNAPSHOT

Description:

Product type:

Indication:

Research collaborator:

Commercial partner: Development status: Next project milestone:

Patent status:

Vascular Endothelial Growth Factor B (VEGF-B) gene and protein therapies Gene therapy and recombinant

protein therapy

Cardiovascular disease

Queensland Institute of Medical Research/Ludwig Institute for

Cancer Research

Currently seeking a partner Preclinical

Partnering

Granted in Australia, Canada, Europe and the US. Pending in Japan and

other countries.

Despite a multitude of strategies aimed at reducing the incidence. heart attacks remain common. In the US, heart attacks are the single leading cause of death with approximately 1.1 million occurring each year. Acute blockage of the blood vessels which supply oxygeri to the heart muscle (the coronary arteries) is the major cause of heart attacks. This acute blockage is usually a consequence of a previous narrowing of the coronary arteries due to atherosclerosis.

Various strategies have been explored to overcome the narrowing of coronary arteries due to atherosclerosis. These include blood vessel grafts to bypass the narrowed arteries, and more recently, the insertion of stents to hold a narrowed aftery open so as to maintain good blood flow. These strategies, while effective, are limited by the morbidity of the procedures and the risk of the vessels narrowing again.

### Therapeutic Potential

An alternative or complementary strategy to that of bypass grafting or angioplasty is the subject of considerable interest world-wide. Amrad is working on the possibility of encouraging the formation of new blood vessels (angiogenesis or arteriogenesis) to bypass the narrowed vessels that can cause heart attacks. The process of new blood vossel formation is regulated by a variety of cytokines.

The VEGF family of cytokines (VEGF-A, B, C, D and PIGF) have all been shown to be effective in generating new blood vessels and increasing blood flow in animal models. There is the potential to use either VEGF-B protein or the gene for VEGF-B to stimulate the formation of new blood vessels to improve the blood supply to the heart, peripheral organs or muscles.

## CURRENT MARKET AND COMPETITORS

In 2001 an estimated 12,4 million patients in the US were diagnosed with some form of coronary artery disease. The cardiovascular drug market is the largest pharmaceutical market in terms of annual global sales; with estimates in the range of around US\$30 billion.

Although no gene or protein therapies are currently available to help patients with cardiovascular disease, there are several gene therapies in development, the most advanced being Schering's (Generex) As5-FGF-4, which is currently in Phase III clinical trials. Once on the market, gene and protein therapies have the potential to offer coronary artery disease patients an alternative to existing treatments, particularly in patients where the disease is detected early.

## Commercial Strategy

Until mid 2003 Amrad's VEGF-B gene therapy project was partnered with GenCell (formerly part of Aventis) and the protein therapy was partnered with Edwards Life Sciences (formerly part of Baxter). Both of these projects completed animal studies with these partners. Amrad is considering its commercial strategy in respect of these projects.

## Project Status

Initial preclinical efficacy studies of the VEGF-B gene and protein in models of peripheral and coronary artery disease have been completed.

#### Scientific Rationale

in vivo growth factor-based stimulation of new blood vossol formation represents a novel experimental approach to the treatment of cardiovascular disease. In various animal models of cardiovascular disease this strategy, called "therapeutic



angiogenesis", has been highly effective, resulting in increased blood flow and, in some cases, improvements in function. Much of this animal work (including clinical trials) has focussed on the various forms of VEGF-A.

Despite evidence of an important role for VEGF-B in heart development and function, direct in vivo evidence of a role for VEGF-B in angiogenesis remains limited. To strengthen this evidence. Amrad and its collaborators have synthesised VEGF-B proteins and developed techniques to deliver the VEGF-B gene. The VEGF-B genc is effective in promoting new blood vesselgrowth in a mouse model of hind-limb ischaemia and in a pigmodel of coronary ischaomia when delivered in a plasmid-based vector. Recombinant VEGF-B protein effectively improves blood supply in a rabbit model of limb ischaemia.

### Suppressors of Cytokine Signalling (SOCS)

Building a therapeutic platform

## SNAPSHOT

Description: Product type: Indication:

Research collaborator:

Commercial partner: Development status: Next project milestone: Patent status:

Suppressors of cytokine signalling (SOCS) inhibitors

Small molecule/antisense/RNAi

Multiple

Cooperative Research Centre for Cellular Growth Factors\*/Walter and Eliza Hall Institute of Medical Research Seeking collaborative partner Research

Lead candidate identified Granted in Australia and the US. Pending in Canada, Europe and Japan.

 The Cooperative Research Centre for Cellular Growth Factors term expired at the end of June 2004.

Cytokines regulate key physiological processes, including growth and responses to injury and infection. However, if expressed inappropriately, cytokines can mediate severe and debilitating disease. Members of the Suppressors of Cytokine Signalling (SOCS) family are expressed in response to many cytokines, including the interferons (used for treatment of chronic hepatius and multiple sclerosis) and granulocyte colony stimulating factor (G-CSF, used for treatment of neutropenia) and interact with receptors or other signalling intermediates to turn off the signalling process and prevent excessive signalling.

## Therapeutic Potential

Current cytokine-based products are proteins and suffer from a number of drawbacks, including the inability to administer them orally, painful injections, poor clinical responses in some cases (possibly related to resistance) and high costs. The SOCS technology platform potentially provides a means to develop novel drugs that mimic cytokine function and would provide an alternative to these protein-based products.

## CURRENT MARKET AND COMPETITORS

Protein-based drugs, for which SOCS antagonists may prove to be an alternative, currently command aggregate sales in excess of US\$15 billion per annum. Products based on the SOCS platform, particularly oral small molecule SOCS antagonists, would be expected to capture a share of these markets due to ease of administration and, possibly, enhanced therapeutic effect. Potential therapeutic targets include:

### SOCS1

### Interferon (IFN) Market

IFN-a is used to treat carrier and chronic hepatitis infection and IFN-B is widely used to treat multiple sclerosis. The combined market for these two interferons is estimated to be in excess of US\$4.5 billion per annum.

### SOCS2

## Muscle Wasting/Growth Disorders Market

Recombinant growth hormone (GH) and Insulin-like Growth Factor 1 (IGF-1) are currently being used or tested clinically to treat growth disorders, muscle-wasting conditions, ostooporosis, and bone fractures. For example, human GH is used clinically as a hormone replacement therapy and also to prevent muscle wasting in conditions such as AIDS. The market for GH is in excess of US\$1 billion. Although the market is highly fragmented, Generatech is the current market leader in the US with sales of almost \$300 million in 2002.



### SOCS3

#### Neutropenia Market

Up to half of cancer chemotherapy patients develop severe neutropenia (low white blood cell count), placing them at risk of contracting life-threatening infections, G-CSF is used in selected patients to help rapidly restore neutrophil (white blood cell) levels to protect patients from infections, with worldwide sales in excess of US\$2 billion per annum. However, on average, less than 10 per cent of chemotherapy patients currently receive proactive protection from neutropenia. Many cancer patients who develop neutropenia will either have their chemotherapy postponed or their dose decreased, both of which impact on survival rates.

#### Obesity Market

Obesity affects almost 60 million adults in the US and leads to an increased risk of illness, including Type II diabetes and hypertension, which in turn lead to cardiovascular diseases and stroke, SOCS3 has been implicated in obesity and SOC3 inhibitors may prove useful the management of obesity.

### Commercial Strategy

In order to exploit the accrued scientific expertise and validation of key SOCS targets, Amrad envisages a collaborative relationship with a partner possessing complementary skills in high throughput screening and downstream lead optimisation, with the aim of identifying small molecular regulators of the SOCS proteins. While Amrad has experience in lead optimisation, the Company hopes to focus primarily on target validation for additional SOCS family members and subsequent development of molecular and cell-based high throughput assays for use in drug discovery.

## Project Status

The aim of Amrad's SOCS research program is to understand the function and biological importance of the SOCS family of proteins in order to identify potential therapeutic applications of SOCS modulators. In particular, gene knockout studies have been performed in mice to validate the SOCS targets.

Drug discovery activities to date have included high throughput screen design and subsequent screening of natural product and defined chemical libraries. A number of active compounds identified using these screens are currently being reviewed for possible progression. Cell-based screening strategies for SOCS protein antagonists have also been developed.

#### Scientific Rationale

Cytokines act by binding to and activating cell-surface receptors and this triggers events within the cell that ultimately lead to functional outputs such as proliferation or survival. SOCS proteins are also produced inside the cell as a consequence of cytokinereceptor binding. By interacting with receptors, or parts of the receptor signalling pathway, the SOCS proteins provide a 'stop' mechanism that prevents the detrimental effects known to be associated with excessive cytokine action.

At least 20 related proteins have been identified within the SOCS family to date. Although little is known about the role of many of these proteins, Amrad, together with its research collaborators, has successfully characterised the functions of SOCS1, SOCS2 and SOCS3. From the evidence currently available it is already clear that molecules which regulate SOCS activity could prove useful for the treatment of a range of conditions including cancer, inflammatory diseases, immunological disorders and other diseases involving cytokine signalling.

#### Anti-infectives Research and Development

As foreshadowed at Amrad's 2003 Annual General Meeting, Amrad has implemented a strategy to separate its biologicals and anti-infectives research into two independent businesses. Amrad will spin-out the anti-infectives portfolio into a new corporate entity, Avexa Limited (Avexa), as detailed in the 5 July 2004 Information Memorandum issued to Arnrad shareholders. This strategy establishes Avexa as an anti-infectives company with a clear focus on treatments for Hepatitis B (HBV), Human Immunodeficiency Virus (HIV) and antibiotic-resistant bacteria.

## Avexa Commercial Strategy

The following is an overview of Avexa's primary research and development programs which Avexa aims to progress to the point of proof-of-concept in animals. If the results at the conclusion of proof-of-concept animal studies are positive. Avexa will seek to raise additional capital to progress the programs to final stage pre-clinical and clinical development. In parallel with continued clinical development, potential commercial partners will be sought to develop pharmaceuticals for sale on world markets.



Project: HBV Non-Nucleoside Antiviral Drugs A new class of drugs for chronic Hepatitis B intection.

## SNAPSHOT

New Drugs for treatment of chronic Description:

**HBV** infection

Product type: Small Molecule Inhibitor Indication:

Treatment of chronic HBV infection Research collaborator: Victorian College of Pharmacy Current development status: Lead compound in efficacy models Next project milestone: Commence formal proclinical toxicalouv

Patent status: Provisional patent stage.

infection with HBV is a serious problem throughout the world. with an estimated 400 million persons infected worldwide. In the US it is estimated that there are around 200,000 new infections of HBV every year, with similar numbers in Europe. The numbers of persons infected with HBV continues to rise despite attempts to prevent the spread of the virus by vaccination.

Chronic HBV infection has been termed 'the silent disease', as the majority of infected individuals have few clinical symptoms initially and may be unaware of their disease for many years. The diagnosis of chronic HBV infection is often not made until the clinical signs of liver disease become apparent, possibly decades after the initial infection. The long asymptomatic phase coupled with the slow development of the disease has resulted in chronic HBV infection not being perceived as such an immediate health threat as HIV. Nonetheless, chronic HBV infection is a serious disease causing progressive liver damage. Between 25 per cent and 40 per cent of chronically infected people will die prematurely from liver disease and/or liver cancer without treatment. The treatment of chronic HBV is as yet still in its infancy but is steadily evolving.

As long term data becomes available on the clinical and economic benefits of antiviral treatment in reducing the progression of liver disease (and hence the need for liver transplantation), more aggressive treatment of chronic HBV is anticipated. The introduction of new, more effective, therapies will also increase treatment options and allow the development of combination therapies, as previously seen in the HIV market.

### Therapeutic Potential

The introduction of the specific HBV antiviral drugs Zeffix<sup>™</sup> (31C) and Hepsera® (adefovir) is changing the profile of HBV infection into a treatable disease which can be slowed and possibly reversed with early diagnosis and treatment. However, there is only one class of antiviral drugs available on the market or in development for the treatment of HBV. This class of drugs is the nucleoside analogues, of which Zeffix® and Hepsera® are currently approved. Interferon alpha is also used, but is poorly effective, difficult to administer (requiring injections) and has a number of undesirable side effects. Whilst current treatment is partially effective, around 75 per cent of patients develop resistance to Zeffix<sup>®</sup> after three years of treatment. Optimum treatment of chronic HBV will require the use of combinations of drugs from different classes, which target different aspects of viral replication, as used to control HIV infection. However, all drugs currently being developed for treatment of HBV belong to the same class (nucleosides) and hit the same target (the polymerase) as Zeffix<sup>®</sup>. Non-nucleoside inhibitors of HBV would have great therapeutic potential as a new class of HBV drugs for use both alone and in combination with existing drugs.

## **CURRENT MARKET AND COMPETITORS**

The HBV-targeted annual sales of Zeffix and Interferon alpha are difficult to estimate because these drugs are also used to treat other diseases. Hepsora<sup>®</sup>, a nucleoside analogue used exclusively for HBV. was first launched in 2003 and achieved sales of USS50 million for its first partial year. Gilead Sciences, the marketer of Hepsera® estimates the HBV drug market to be worth in excess of US\$500 million. Currently there are approximately one million chronic HBV sufferers in the US and around three million sufferers in Europe. The introduction of new drugs, coupled with improved diagnosis and increased awareness of the long term:clinical and economic benefits of antiviral treatment, will drive future expansion of this market. Avexa is developing non-nucleoside drugs against novel HBV targets which, if successful, could deliver products that are 'first in class' with correspondingly high market potential.

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### Current launched and HBV drugs

Brand	Intron A <sup>®</sup>	Zeffix <sup>®</sup>	Hepsora <sup>re</sup>
Generic	Interferon-alpha	Lamivudine (31C)	Adefovir
Marketer	Shering-Plough	GSK/Shire Pharmaceuticals	Gilead Sciences
Drug class	Interferon	Polymorase inhibitor	Polymerase inhibitor
Sales 2003 US \$millions	~150	- 200	-50 (launched 2003)

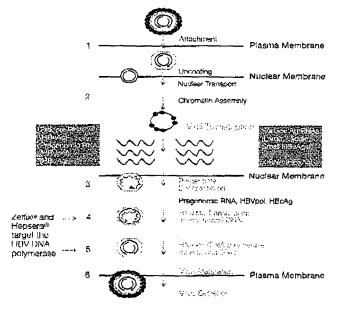
## Project Status

A candidate drug has been selected and will enter an animal efficacy model of HBV infection in the third quarter of 2004.

#### Scientific Rationale

The replication cycle of HBV contains several steps which are essential for viral replication and are therefore good targets for the discovery of anti-HBV drugs. The major steps are shown in the diagram below. However, the RT/DNA polymerase of HBV (steps 4 and 5) is the only component of the HIV replication cycle which has been targeted by existing drugs such as the nucleoside analogues Zeffix<sup>®</sup> and Hepsera<sup>®</sup>. Avexa's compounds are not nucleoside analogues and do not affect the same target as Zeffix<sup>36</sup>/ Hepsera<sup>66</sup>; they are a new class of inhibitors of HBV replication.

#### Steps in the HBV life cycle



## Project: HIV Integrase Inhibitors

A major new drug targe, for HIV infection

SNAPSHOT	
Description:	New class of drugs for treatment of HIV infection
Product type:	Small Molecule Inhibitor
Indication:	Treatment of HIV infection
Research collaborator:	Victorian College of Pharmacy
Current development status:	Lead optimisation
Next project milestone:	Lead selected for animal model
Patent status:	Provisional patent stage.

Recent World Health Organisation statistics reveal HIV has become the fourth largest cause of death globally. There are an estimated 40 million HIV sufferers worldwide, with around 900,000 in the US and 600,000 in Western Europo. While the greatest incidence of HIV is in developing countries, HIV still represents a significant health problem in the Western world. Each year in the US an estimated 40,000 new patients with HIV infection are registered for treatment, with most receiving a combination of drugs.

Although the introduction of antiviral drugs has improved the life expectancy and reduced disease progression, the virus rapidly becomes resistant to these drugs. Around 270,000 patients in the US are resistant to at least one class of HIV drug, and around 50,000 have developed resistance to all three current drug classes. In addition, up to 20 per cent of new infections now involve the transmission of resistant virus, resulting in new classes of antiviral drugs (especially against new targets) providing the only hope of treatment for an increasing number of patients.

## Therapeutic Potential

In addition to new classes of drugs to overcome resistance, there is also a need for new drugs with an improved side-effect profile and/or easier administration. Many of the present HIV drugs have serious side-effects which for some patients are intolerable. The complicated dosing regimen of some drug combinations and the large number of pills also impose significant burdens on the patient. An attempt to alleviate these treatment difficulties has led to the introduction of single combination pills such as Trizivir®, containing three separate nucleoside reverse transcriptase inhibitors (NRTIs) in a single pill.

Since the development of the first HIV reverse transcriptase inhibitors, new classes of inhibitors (such as the protease inhibitors and the non-nucleoside inhibitors) have been developed. and each new class has expanded the total HIV market as patients are treated with several drugs simultaneously. In addition to new drug classes, several additional drugs in the same existing classes have been successfully developed, with each capturing

significant market share. To date there is no integrase inhibitor on the market. Given the success of drugs that inhibit the two other HIV enzymos (reverse transcriptase and professe), there is every reason to believe that the first, second, third and following integrase inhibitors to reach the market will achieve significant sales.

## CURRENT MARKET AND COMPETITORS

HIV therapies share a multi-billion dollar market, with drugs such as Combivir® (Jaunched 1997) and Kaletra® (Jaunched 2000) each generating approximately US\$800 million in sales per year. While the first market entrants in a particular drug class tend to achieve the highest sales, new drugs in an existing class can generate significant revenues if they have a better clinical profile. A recent example is Gilead's Viread®, an NRTI which was launched in late 2001 and the seventh NRTI to reach the market. Sales of Viread® in 2003 were in excess of US\$500 million. Even as a late entrant Virgad has proven successful because of its superior efficacy against the resistant strains that have emerged to the older NRTIs. As a new class of drugs, the first three or four integrase inhibitors to reach the market are very likely to match the success' of Vircad® and generate around US\$500 million in sales. At present there are no integrase inhibitors in clinical development for treatment of HIV.

## Project Status

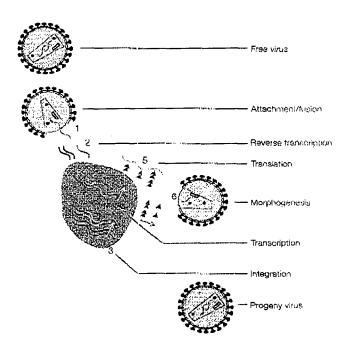
A series of lead compounds has been generated through high throughput screening assays and these compounds are presently being optimised using comprehensive cellular assays and rnolecular modelling techniques to select a lead molecule for preclinical testing.

## Scientific Rationale

The replication cycle of HIV contains several enzymes/processes which are essential for viral replication and which are therefore good targets for the discovery of anti-HIV drugs. The major steps

are shown in the diagram below. Effective inhibitors have been developed to target the fusion event (Step 1), the reverse transcriptase (RT) enzyme (Step 2) and the protease (PR) enzyme (Step 6). HIV integrase is the third enzyme encoded by HIV, and Avexa expects inhibitors of HIV integrase may be as successful at controlling HIV disease as the RT and PR inhibitors already on the market.

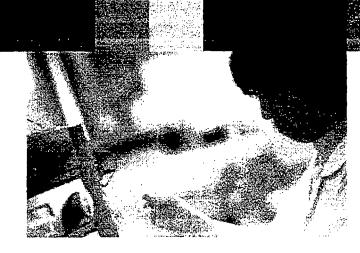
### Stops in the HIV life cycle



#### Launched HIV treatments and 2003 sales

Class	Brarid name	Generic harne	1st launch	Marketor	2003 worldwide sales US\$ millions
NRTI"	Zerit <sup>%</sup>	stavudine/d4T	1994	BMS .	354
NRTI'	Epivir <sup>®</sup>	lamivudine (3TC)	1995	GSK	498
NRTI	Viread <sup>(v)</sup>	tenofovir	2002	Gilcad Sciences	566
NRTI*	Emtriva**	emtricitabine	2003	Triangle/Gilead Sciences	10
NNRTI"	Sustiva b	efavirenz	1998	BMS	752
Entry inhibitor	Fuzeon®	enfuvirlide	2003	Trimeris/Roche	36
Combo*** (NRTI*)	Ĭrlzivir <sup>‡0</sup>	epivir (3TC), retrovir (AZT) and abacavir	2000	GSK	640
Combo" (NRTI')	Combivir <sup>®</sup>	epivir (3TC) and retrovir (AZT)	1997	GSK	1000
Combo (PR***)	Kaletra <sup>®</sup>	(opinavir/ritonavir	2000	Abbott	740

- NRTI Nucleoside reverse transcriptase inhibitor
- NNRTI Non-nucleoside reverse transcriptase inhibitor
- Combo Fixed dose combination
- \*\*\*\* PR Protease inhibitor



Project: Vancomycin- and Methicillin-Resistant Bacterial Infections

A treatment for ontreatable 'superbugs'

### **SNAPSHOT**

Description:	Drugs for treatment of antibiotic- resistant bacteria
Product type:	Small Molecule Inhibitor
Indication:	Treatment of antibiotic-resistant
	bacterial infections
Research collaborator:	University of Wollongong:
Current development status:	Lead optimisation
	Lead selected for animal model
Patent status:	National/Regional Phase for
•	United States, Europe, Canada,
4	and Australia

Cases of severe bacterial infections that are resistant to current anti-bacterial drugs are becoming more and more frequent. Many of these are acquired within hospitals themselves. Five to ten percent of patients admitted to hospital in the United States develop some level of hospital acquired infection. Of these approximately nine per cent die from bacterial infection and associated complications. An estimated 90,000 people in the United States died from hospital-acquired infections in 1999, almost 50 per cent more than diabetes. Staphylococcus aureus infects about 400,000 United States hospital patients a year, and about one-quarter of these die from the infection.

## Therapeutic Potential

The development of bacterial resistance to antibiotics has resulted in continued market opportunities for new compounds which act against resistant strains of bacteria. Only one new class of antibiotics (Zyvox<sup>®</sup>) has been marketed in the last 35 years. and resistance to this drug has already been described. The present drug of last resort, when all else fails, is vancomycin. However, vancomycin-resistant bacteria are spreading, and there is currently no simple antibiotic treatment for vancomycinresistant infections, creating a significant unmet medical need that is likely to continue to expand in the future.

## CURRENT MARKET AND COMPETITORS

Worldwide sales of anti-bacterial products reached US\$28 billion in 2002. Newly lauched antibiotics typically generate US\$300-500 million in sales annually, rising to >US\$1 billion for products such as Rocephin®, Several anti-bacterial compounds are currently being developed by competitors, but, without exception, all are directed against targets that are likely to be vulnerable to single gene mutations leading to rapid development of antibacterial resistance and a resulting loss of activity and competitive position. In contrast this project is developing compounds against a different target on the bacteria than other competitor compounds. Hence these load compounds would still be expected to retain activity against bacteria resistant to competitor compounds.

Drugs in development for antibiotic resistant bacteria

Drug	Developer	Status Marke	t size estimates \$US millions
Zyvox <sup>(\$</sup>	Pharmacia	Launched	379 (2004)
Synercid®	Aventis	Launched	77 (2004)
Cidecin <sup>66</sup>	Cubist/Gilead Sciences	Approved	325 (2005)
Ramoplanin	Biosearch Italia/ Genome Therapeutics	Phase III	300 (2007)
RWJ-54428	J&J. Essential Therapeutics	Phase I	

## Project Status

A series of lead compounds has been generated through molecular modelling and directed medicinal chemistry, and these compounds are presently being optimised using antibacterial assays and molecular modelling techniques to select a lead molecule for preclinical testing.



### Scientific Rationale

Resistance to varicomycin occurs when bacteria are able to change their cell wall such that vancomycin can no longer bind to the modified bacterial cell wall. Rather than search for new compounds against normal bacteria in the hope that they might retain activity against resistant bacteria, this project set out to design compounds that actively bind to the modified cell wall in resistant bacteria, using structural information from the vancomycin-resistant cell wall in the design process. This novel approach has required the development of new chemistry to synthesise compounds capable of binding to the modified target (as well as the normal target). This has resulted in a novel series of synthetic compounds which would not be identified by any traditional screening process. These compounds show antibacterial activity against both vancomycin sensitive and vancomycin-resistant bacteria, as the compounds can bind to both the normal and the modified (resistant) cell wall, and stop the bacteria from growing.

## Trademark ownership acknowledgements

Avastin<sup>66</sup> is a registered trademark of Genentech, Inc.

Cidecin<sup>®</sup> is a registered trademark of Cubist Pharmaceuticals, Inc. Combivir®, Epivir®, Trizivir®, Zettix $^{6}$  and Ziagen $^{6}$  are registered trademarks of Glaxo Group Limited.

Emtriva™ is a trademark and Hepsera® and Viread® are registered trademarks of Gilead Sciences, Inc.

Enbrei<sup>®</sup> is a registered trademark of Wyeth.

Fuzeon®, Mab Thera® and Rocephin® are registered trademarks of Hoffman-La Roche Inc.

Humira® and Kaletra® are registered trademarks of Abbott Laboratories Inc.

Intron  $\Lambda^{\otimes}$  is a registered trademark of Schering-Plough Corporation.

Remidade<sup>60</sup> is a registered trademark of Centodor, Inc.

Rituxan<sup>46</sup> is a registered trademark of idea Pharmacouticals Corporation,

Sustiva  $^{\oplus}$  and Zerit  $^{\oplus}$  are registered tradernarks of Bristol-Myers Squibb Pharma Company.

Synercid<sup>®</sup> is a registered trademark of Aventis Pharma SA.

Xolair® is a registered trademark of Novartis AC.

Zyvoxie is a registered trademark of Pharmacia/Upjohn Caribo, Inc.

The Amrad Board is committed to maintaining the highest ethical standards and best practice in the area of corporate governance. within the framework of the Australian Stock Exchange Corporate Governance Council Principles of Good Corporate Governance and Best Practice Recommendations (ASX Guidelines) to ensure the Company's business is conducted in the best interests of all stakeholders.

### Shareholders

The Board is committed to delivering maximum share value to the Company's shareholders while maintaining high standards of employment, full compliance with relevant legislation and meeting the Company's responsibilities to all stakeholders.

The Board recognises the importance of keeping shareholders fully informed of the Company's activities by providing relevant and useful information to all shareholders in a timely manner. Shareholders play an integral role in the governance of the Company by electing Directors. At every Annual General Meeting (AGM) the longest serving third of the Board of Directors retires (excluding any Chief Executive Officer/Executive Director) and may seek re-election to the Board. New Directors appointed by the Board must also stand for election at the Company's next AGM.

The principal method of communicating to shareholders is through the Company's Annual Report, issued to all shareholders and posted on the Company's website. Company announcements are posted on the Company website and shareholders can register through the website to receive notification of all announcements made. In addition, through the Company's AGM, shareholders receive reports by the Board on Amrad's activities for consideration and can participate by attending the meeting.

## Role of the Board

The Board is responsible to shareholders for the performance of the Company and for the overall corporate governance of Amrad. This role encompasses the determination of Amrad's goals and strategic direction and ensures timely and accurate communications to shareholders. The Board has established policies in respect of Board responsibilities and delegations of authority for the appropriate management of the Company's

The Board has also adopted management policies and procedures addressing statutory financial reporting, Board and management financial reporting and controls, information technology security, contract management, management and staff performance reviews and remuneration, internal controls for business risk management, ethical standards and occupational health and safety practices.

The Board is responsible for appointing the Chief Executive Officer and reviewing his or her performance. The Chief Executive Officer is responsible for the overall implementation and management of the policies and strategies established by the Board.

### **Board Composition**

The Board is currently composed of five Non-executive Directors and one Executive Director.

Amrad's Constitution specifies that the number of Directors shall not be less than three or more than nine. At present the Board consists of:

Mr Bob Moses Chairman

Appointed a Director 21 May 2002 and as Chairman 16 October 2003

Dr Peter Smith

Chief Executive Officer/Executive Director

Appointed 16 October 2003

Ms Helen Cameron

Non-executive Director

Appointed 18 December 1997

Professor Silviu Itescu

Non-executive Director

Appointed 17 July 2003

Mr Graeme Kaufman

Non-executive Director

Appointed 17 July 2003

Mr Olaf O'Duill

Non-executive Director

Appointed 21 May 2002 as Chairman and retired as Chairman on 16 October 2003

Professor John Mills, the former Deputy Chairman and Nonexecutive Director, resigned on 15 October 2003 and Amrad's former Managing Director, Dr Sandra N Webb resigned on 8 July 2003.

Amrad's policy governing Board composition requires the Chairman and a majority of the Board to be independent Non-executive Directors. In assessing independence, the Board has regard to the ASX Guidelines and the independence of each Director is monitored by the Board on an ongoing basis in light of disclosed interests. As at the date of this Annual Report the Board has determined that all Amrad Directors are independent, other than Mr Graeme Kaufman a Director of Amrad's majority shareholder. Fibre Optics (Australia) Pty Ltd.

The Board strives to ensure its composition includes an appropriate mix of expertise and experience relevant to Amrad's business activities conducive to making expedient decisions in the best interests of the Company. The relevant skills, experience and expertise of each Board member is set out on pages 21 to 23 of this Annual Report.

A formal performance evaluation for the Amrad Board and its rnembers did not occur during the reporting period. However, the Board has reviewed Board composition and the skill set requirements for Board members. The Board is committed to future annual reviews of its performance, both individually and collectively, as well as annual reviews of key Company management against both measurable and qualitative indicators. A description of the process for performance evaluations is posted on the corporate governance section of the Company's website.

The Board recognises the importance of each Director bringing independent judgement to bear in the Board decision making process. As such, all Directors have access to independent professional advice at the Company's expense with the approval of the Chairman. Directors are also indemnified under the Company's Constitution, and in accordance with deeds of indemnity and insurance on terms approved by the Company's shareholders.

#### Board Committees

Two Board Committees facilitate the execution of the Board's responsibilities:

### Corporate Governance and Nominations Committee

The role of the Corporate Governance and Nominations Committee is to address corporate governance matters and to source potential Directors.

The members of this Committee during the period 1 July 2003 to 30 June 2004 were:

- Mr Bob Moses (Chairman)
- Ms Helen Cameron
- Professor Silviu Itescu

The Directors attended one Committee meeting held during the above period.

### Board Audit Compliance and Risk Management Committee

The Board Audit Compliance and Risk Management Committee (BACRMC) is responsible for all matters relating to the assets and financial affairs of the Company and its subsidiary companies. including internal and external audit issues. The specific responsibilities of the BACRMC include compliance with financial statutory reporting requirements, monitoring internal control systems, review and assessment of external audit matters, overseeing the independence of the Company's external auditors. review of Company insurance cover, risk management processes and other matters referred by the Board. The BACRMC charter is posted on the corporate governance section of the Company's website.

The Board also requires the provision of written assurances in respect of the accuracy and compliance of Company finance reports by the Chief Executive Officer and the Director, Finance and Administration as part of the management sign-off process for the half year and full year Company financial statements.

As a result of Board composition changes during the reporting period, the Company has not complied with the ASX Guidelines in respect of the structure of the BACRMC in so far as there must be at least three members and the requirement for a majority of independent Directors. At the present time only one independent Non-executive Director sits as a member of the BACRMC.

The members of the BACRMC during the period 1 July 2003 to 30 June 2004 were:

- Ms Helen Cameron (Chairman)
- Professor John Mills, resigned 15 October 2003
- Mr Graeme Kaufman, appointed 17 July 2003
- Mr Bob Moses, resigned 17 July 2003
- · Mr Qlaf O'Duill, ex officio

Four BACRMC meetings were held during the above period and details of Directors' attendances are set out on page 25 of this Annual Report.

## Other committees

Having regard to the size of the Board and the nature and extent of the Company's requirements in relation to remuneration issues, the Board has determined that a Board remuneration committee is not currently warranted. All matters pertaining to the remuneration of the Board, management and employees are considered by the full Board of Directors.

Other sub-committees are established by the Board on an as needs basis from time to time to monitor specific Company transactions and projects, in March 2004 the Board established a share buy-back committee following the announcement of the Company's share buy-back program.

#### Ethical standards and compliance

Amrad prescribes ethical standards for employees for professional conduct, dealings with the business community, the public and with other employees

The Company has adopted policies and guidelines in the context of both the applicable legislation and accepted community standards. The Board has determined not to implement a separate code of conduct in respect of these matters, but rather to articulate the Company's requirements for standards of conduct in individual policies dealing with relevant issues including confidentiality, conflicts of interest, fraud risks, employee discrimination and harassment, and trading in Company securities.

## Trading of Company Securities by Directors and Employees

Company policy prohibits the trading of Company securities by Directors and employees whilst in possession of price sensitive information. A summary of Amrad's policy is posted on the corporate governance section of the Company's website.

## Market Disclosure

As a public listed company, Amrad is required to comply with ASX Listing Rules continuous disclosure obligations, as complemented by the Corporations Act disclosure requirements. A summary of Amrad's policy and continuous disclosure procedures is posted on the corporate governance section of the Company's website.

## Company Auditor

KPMG has been Amrad's external auditor since the Company was incorporated in 1986. KPMG meets at least four times each year with the Board Audit Compliance and Risk Management Committee and is given the opportunity to meet with Amrad Directors without management in attendance. A representative from KPMG attends Amrad's AGM.

Information on procedures for the selection and appointment of the Amrad's external auditor and rotation of the audit engagement partner are posted on the corporate governance section of the Company's website.

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# CORPORATE GOVERNANCE

CONTINUED



#### Risk Management

The risks associated with Amrad's business are wide ranging and include the following:

- long lead times and high costs involved in R&D, with no guarantee of success:
- complex government and health regulations which are subject to change;
- · uncertainty in obtaining approval to market a pharmaceutical product;
- · the high level of funding required over a long period of time; and
- securing rights to technology and patents as an integral part of obtaining potential product value.

Shareholder value analysis is considered by the Board to be integral to the management of Amrad's business and its related risks, with the objective of maximising shareholder returns over

The consideration and approval by the Board each year of the Company strategy, business plans and financial budgets involve identification of significant risks and the implementation of appropriate strategies to deal with them. Following the adoption of the Company's strategic risk management framework the Company has implemented a risk management plan which is reviewed by the Board and management on at least an annual basis. The Board also receives monthly detailed reports and briefings by management on the Company's financial performance, research and development programs and business development activities. Occupational health, safety and rehabilitation reports and environmental compliance reports are also submitted by management and monitored by the Board on a regular basis. Details of Amrad's risk management policy and internal systems are posted on the corporate governance section of the Company's website.

## Executive Remuneration

Company remuneration policies and practices including details of shares and/or options issued under Amrad's Employee Share Ownership Plan and/or the Key Employee Share Option Plan are set out on pages 28 to 30 of this Annual Report. Copies of the share and option plans are posted on the corporate governance section of the Company's website.

Corporate performance targets have been established for Amrad's Chief Executive Officer, Dr Peter Smith, as part of his remuneration arrangements. Shareholder approval will be sought at the 2004 AGM to issue Dr Smith 600,000 options to subscribe for ordinary shares in the capital of the Company through an Option Incentive Plan. The options offered to Dr Smith will be divided into three tranches of 200,000 options exercisable progressively over three year periods as detailed in the explanatory notes to the 2004 AGM Notice.

Particulars of the remuneration of the former Managing Director, Dr Webb, and each of the highest paid Company management. Executives including the Chief Executive Officer, Dr Smith, for the period 1 July 2003 to 30 June 2004, including all monetary and non-monetary components, are set out on page 29 of this Annual Report.

#### Non-executive Directors Remuneration

Remuneration of Non-executive Directors is determined in aggregate by shareholders in general meeting. The Board of Directors determines individual fees within the current \$500,000 aggregate level, having regard to the number of Directors and their respective roles and responsibilities.

Non-executive Directors participate in the Company's Nonexecutive Director Share Plan, established in November 2000. Amrad Non-executive Directors' remuneration is limited to Directors' fees and a contribution to superannuation. Particulars of the remuneration of each Amrad Non-executive Director for the period 1 July 2003 to 30 June 2004, including all monetary and non-monetary components, are set out on page 29 of this Annual Report.